

Offic européen d s brevets



EP 1 108 790 A2 (11)

(12)

# **EUROPEAN PATENT APPLICATION**

- (43) Date of publication: 20.06.2001 Bulletin 2001/25
- (21) Application number: 00127688.0
- (22) Date of filing: 18.12.2000

- (51) Int CI.7: C12Q 1/68, C07H 21/04. C12N 15/63, C07K 14/34, C12R 1/15, G06F 17/00. C12R 1/13, G01N 33/50
- (84) Designated Contracting States: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR Designated Extension States: AL LT LV MK RO SI
- (30) Priority: 16.12.1999 JP 37748499 07.04.2000 JP 2000159162 03.08.2000 JP 2000280988
- (83) Declaration under Rule 28(4) EPC (expert solution)
- (71) Applicant: KYOWA HAKKO KOGYO CO., LTD. Chiyoda-ku, Tokyo 100-8185 (JP)
- (72) inventors:
  - Nakagawa, Satochi, c/o Kyowa Hakko Kogyo Co.,Ltd. Machida-shi, Tokyo 194-8533 (JP)
  - Mizoguchi, Hiroshi, c/o Kyowa Hakko Kogyo Co.,Ltd. Machida-shi, Tokyo 194-8533 (JP)

- Ando, Seiko, c/o Kyowa Hakko Kogyo Co., Ltd. Machida-shi, Tokyo 194-8533 (JP)
- Hayashi, Mikiro, c/o Kyowa Hakko Kogyo Co.,Ltd. Machida-shi, Tokyo 194-8533 (JP)
- Ochiai, Keiko, c/o Kyowa Hakko Kogyo Co.,Ltd. Machida-shi, Tokyo 194-8533 (JP)
- Yokoi, Haruhiko, c/o Kyowa Hakko Kogyo Co.,Ltd. Machida-shi, Tokyo 194-8533 (JP)
- Tateishi, Naoko. c/o Kyowa Hakko Kogyo Co.,Ltd. Machida-shi, Tokyo 194-8533 (JP)
- Senoh, Akihiro, c/o Kyowa Hakko Kogyo Co.,Ltd. Machida-shi, Tokyo 194-8533 (JP)
- ikeda, Masato, c/o Kyowa Hakko Kogyo Co.,Ltd. Machida-shi, Tokyo 194-8533 (JP)
- Ozaki, Akio, c/o Kyowa Hakko Kogyo Co., Ltd. Hofu-shi, Yamaguchi 747-8522 (JP)
- (74) Representative: VOSSIUS & PARTNER Siebertstrasse 4 81675 München (DE)

#### (54)Novel polynucleotides

Novel polynucleotides derived from microorganisms belonging to coryneform bacteria and fragments thereof, polypeptides encoded by the polynucleotides and fragments thereof, polynucleotide arrays

comprising the polynucleotides and fragments thereof, recording media in which the nucleotide sequences of the polynucleotide and fragments thereof have been recorded which are readable in a computer, and us of them.

EP 1 108 790 A2

#### **Description**

5

10

15

20

25

30

35

40

45

50

55

### BACKGROUND OF THE INVENTION

#### 1. Field of the Invention

[0001] The present invention relates to novel polynucleotides derived from microorganisms belonging to coryneform bacteria and fragments thereof, polyneptides encoded by the polynucleotides and fragments thereof, polynucleotide arrays comprising the polynucleotides and fragments thereof, computer readable recording media in which the nucleotide sequences of the polynucleotide and fragments thereof have been recorded, and use of them as well as a method of using the polynucleotide and/or polypeptide sequence information to make comparisons.

## 2. Brief Description of the Background Art

[0002] Coryneform bacteria are used in producing various useful substances, such as amino acids, nucleic acids, vitamins, saccharides (for example, ribulose), organic acids (for example, pyruvic acid), and analogues of the above-described substances (for example, N-acetylamino acids) and are very useful microorganisms industrially. Many mutants thereof are known.

[0003] For example, Corynebacterium glutamicum is a Gram-positive bacterium identified as a glutamic acid-producing bacterium, and many amino acids are produced by mutants thereof. For example, 1,000,000 ton/year of L-glutamic acid which is useful as a seasoning for umami (delicious taste), 250,000 ton/year of L-lysine which is a valuable additive for livestock feeds and the like, and several hundred ton/year or more of other amino acids, such as L-arginine, L-proline, L-glutamine, L-tryptophan, and the like, have been produced in the world (Nikkei Bio Yearbook 99, published by Nikkei BP (1998)).

[0004] The production of amino acids by *Corynebacterium glutamicum* is mainly carried out by its mutants (metabolic mutants) which have a mutated metabolic pathway and regulatory systems. In general, an organism is provided with various metabolic regulatory systems so as not to produce more amino acids than it needs. In the biosynthesis of Llysine, for example, a microorganism belonging to the genus *Corynebacterium* is under such regulation as preventing the excessive production by concerted inhibition by lysine and threonine against the activity of a biosynthesis enzyme common to lysine, threonine and methionine, i.e., an aspartokinase, (*J. Biochem., 65*: 849-859 (1969)). The biosynthesis of arginine is controlled by repressing the expression of its biosynthesis gene by arginine so as not to biosynthesize an excessive amount of arginine (*Microbiology, 142*: 99-108 (1996)). It is considered that these metabolic regulatory mechanisms are deregulated in amino acid-producing mutants. Similarly, the metabolic regulation is deregulated in mutants producing nucleic acids, vitamins, saccharides, organic acids and analogues of the above-describ d substances so as to improve the productivity of the objective product.

[0005] However, accumulation of basic genetic, biochemical and molecular biological data on coryneform bacteria is insufficient in comparison with *Escherichia coli, Bacillus subtilis,* and the like. Also, few findings have been obtain d on mutated genes in amino acid-producing mutants. Thus, there are various mechanisms, which are still unknown, of regulating the growth and metabolism of these microorganisms.

[0006] A chromosomal physical map of *Corynebacterium glutamicum* ATCC 13032 is reported and it is known that its genome size is about 3,100 kb (*Mol. Gen. Genet., 252*: 255-265 (1996)). Calculating on the basis of the usual gene density of bacteria, it is presumed that about 3,000 genes are present in this genome of about 3,100 kb. However, only about 100 genes mainly concerning amino acid biosynthesis genes are known in *Corynebacterium glutamicum*, and the nucleotide sequences of most genes have not been clarified hitherto.

[0007] In recent years, the full nucleotide sequence of the genomes of several microorganisms, such as Escherichia coli, Mycobacterium tuberculosis, yeast, and the like, have been determined (Science, 277: 1453-62 (1997); Nature, 393: 537-544 (1998); Nature, 387: 5-105 (1997)). Based on the thus determined full nucleotide sequences, assumption of gene regions and prediction of their function by comparison with the nucleotide sequences of known genes have been carried out. Thus, the functions of a great number of genes have been presumed, without genetic, biochemical or molecular biological experiments.

[0008] In recent years, moreover, techniques for monitoring expression levels of a great number of genes simultaneously or detecting mutations, using DNA chips, DNA arrays or the like in which a partial nucleic acid fragment of a gene or a partial nucleic acid fragment in genomic DNA other than a gene is fixed to a solid support, have ben developed. The techniques contribute to the analysis of microorganisms, such as yeasts, *Mycobacterium tuberculosis*, *Mycobacterium bovis* used in BCG vaccines, and the like (*Science*, 278: 680-686 (1997); *Proc. Natl. Acad. Sci. USA*, 96: 12833-38 (1999); *Science*, 284: 1520-23 (1999)).

## SUMMARY OF THE INVENTION

[0009] An object of the present invention is to provide a polynucleotide and a polypeptide derived from a microorganism of coryneform bacteria which are industrially useful, sequence information of the polynucleotide and the polypeptide, a method for analyzing the microorganism, an apparatus and a system for use in the analysis, and a method for breeding the microorganism.

[0010] The present invention provides a polynucleotide and an oligonucleotide derived from a microorganism belonging to coryneform bacteria, oligonucleotide arrays to which the polynucleotides and the oligonucleotides are fixed, a polypeptide encoded by the polynucleotide, an antibody which recognizes the polypeptide, polypeptide arrays to which the polypeptides or the antibodies are fixed, a computer readable recording medium in which the nucleotide sequences of the polynucleotide and the oligonucleotide and the amino acid sequence of the polypeptide have been recorded, and a system based on the computer using the recording medium as well as a method of using the polynucleotide and/or polypeptide sequence information to make comparisons.

#### 15 BRIEF DESCRIPTION OF THE DRAWING

10

25

35

40

45

50

55

[0011] Fig. 1 is a map showing the positions of typical genes on the genome of Corynebacterium glutamicum ATCC

[0012] Fig. 2 is electrophoresis showing the results of proteome analyses using proteins derived from (A) Corynebacterium glutamicum ATCC 13032, (B) FERM BP-7134, and (C) FERM BP-158.

[0013] Fig. 3 is a flow chart of an example of a system using the computer readable media according to the pres int

[0014] Fig. 4 is a flow chart of an example of a system using the computer readable media according to the pres nt

## DETAILED DESCRIPTION OF THE INVENTION

[0015] This application is based on Japanese applications No. Hei. 11-377484 filed on December 16, 1999, No. 2000-159162 filed on April 7, 2000 and No. 2000-280988 filed on August 3, 2000, the entire contents of which are incorporated hereinto by reference.

[0016] From the viewpoint that the determination of the full nucleotide sequence of Corynebacterium glutamicum would make it possible to specify gene regions which had not been previously identified, to determine the function of an unknown gene derived from the microorganism through comparison with nucleotide sequences of known genes and amino acid sequences of known genes, and to obtain a useful mutant based on the presumption of the metabolic regulatory mechanism of a useful product by the microorganism, the inventors conducted intensive studies and, as a result, found that the complete genome sequence of Corynebacterium glutamicum can be determined by applying the whole genome shotgun method.

[0017] Specifically, the present invention relates to the following (1) to (65):

## (1) A method for at least one of the following:

- (A) identifying a mutation point of a gene derived from a mutant of a coryneform bacterium,
- (B) measuring an expression amount of a gene derived from a coryneform bacterium,
- (C) analyzing an expression profile of a gene derived from a coryneform bacterium,
- (D) analyzing expression patterns of genes derived from a coryneform bacterium, or
- (E) Identifying a gene homologous to a gene derived from a coryneform bacterium, said method comprising:

(a) producing a polynucleotide array by adhering to a solid support at least two polynucleotides selected from the group consisting of first polynucleotides comprising the nucleotide sequence represented by any one of SEQ ID NOS:1 to 3501, second polynucleotides which hybridize with the first polynucleotides under stringent conditions, and third polynucleotides comprising a sequence of 10 to 200 continuous bases of the first or second polynucleotides,

(b) incubating the polynucleotide array with at least one of a labeled polynucleotide derived from a coryneform bacterium, a labeled polynucleotide derived from a mutant of the coryneform bact rium or a labeled polynucleotide to be examined, under hybridization c nditions,

(c) detecting any hybridization, and

(d) analyzing the result of the hybridization.

As used herein, for example, the at least two polynucleotid is can be at least two of the first polynucleotides, at least two of the second polynucleotides, at least two of the third polynucleotides, or at least two of the first, second and third polynucleotides.

- (2) The method according to (1), wherein the coryneform bacterium is a microorganism belonging to the genus Corynebacterium, the genus Brevibacterium, or the genus Microbacterium.
- (3) The method according to (2), wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium ammoniagenes.
- (4) The method according to (1), wherein the polynucleotide derived from a coryneform bacterium, the polynucleotide derived from a mutant of the coryneform bacterium or the polynucleotide to be examined is a gene relating to the biosynthesis of at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof.
- (5) The method according to (1), wherein the polynucleotide to be examined is derived from Escherichia coli.
- (6) A polynucleotide array, comprising:

5

10

15

20

25

30

35

40

45

50

55

at least two polynucleotides selected from the group consisting of first polynucleotides comprising the nucleotide sequence represented by any one of SEQ ID NOS:1 to 3501, second polynucleotides which hybridize with the first polynucleotides under stringent conditions, and third polynucleotides comprising 10 to 200 continuous bases of the first or second polynucleotides, and a solid support adhered thereto.

As used herein, for example, the at least two polynucleotides can be at least two of the first polynucleotides, at least two of the second polynucleotides, at least two of the third polynucleotides, or at least two of the first, second and third polynucleotides.

- (7) A polynucleotide comprising the nucleotide sequence represented by SEQ ID NO:1 or a polynucleotide having a homology of at least 80% with the polynucleotide.
- (8) A polynucleotide comprising any one of the nucleotide sequences represented by SEQ ID NOS:2 to 3431, or a polynucleotide which hybridizes with the polynucleotide under stringent conditions.
- (9) A polynucleotide encoding a polypeptide having any one of the amino acid sequences represented by SEQ ID NOS:3502 to 6931, or a polynucleotide which hybridizes therewith under stringent conditions.
- (10) A polynucleotide which is present in the 5' upstream or 3' downstream of a polynucleotide comprising th nucleotide sequence of any one of SEQ ID NOS:2 to 3431 in a whole polynucleotide comprising the nucleotid sequence represented by SEQ ID NO:1, and has an activity of regulating an expression of the polynucleotide.
- (11) A polynucleotide comprising 10 to 200 continuous bases in the nucleotide sequence of the polynucleotide of any one of (7) to (10), or a polynucleotide comprising a nucleotide sequence complementary to the polynucleotide comprising 10 to 200 continuous based.
- (12) A recombinant DNA comprising the polynucleotide of any one of (8) to (11).
- (13) A transformant comprising the polynucleotide of any one of (8) to (11) or the recombinant DNA of (12).
- (14) A method for producing a polypeptide, comprising:

culturing the transformant of (13) in a medium to produce and accumulate a polypeptide encoded by th polynucleotide of (8) or (9) in the medium, and recovering the polypeptide from the medium.

- (15) A method for producing at least one of an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof, comprising:
  - culturing the transformant of (13) in a medium to produce and accumulate at least one of an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof in the medium, and recovering the at least one of the amino acid, the nucleic acid, the vitamin, the saccharide, the organic acid, and analogues thereof from the medium.
- (16) A polypeptide needed by a polynucleotide comprising the nucleotide sequences lected from SEQ ID NOS: 2 to 3431.
- (17) A polypeptide c mprising the amino acid sequence selected from SEQ ID NOS:3502 to 6931.
- (18) The polypeptide according to (16) or (17), wherein at least one amino acid is deleted, replaced, inserted or

added, said polypeptides having an activity which is substantially the same as that of the polypeptide without said at least one amino acid deletion, replacement, insertion or addition.

- (19) A polypeptide comprising an amino acid sequence having a homology of at least 60% with the amino acid sequence of the polypeptide of (16) or (17), and having an activity which is substantially the same as that of the polypeptide.
- (20) An antibody which recognizes the polypeptide of any one of (16) to (19).
- (21) A polypeptide array, comprising:

5

10

15

20

25

30

35

40

45

50

at least one polypeptide or partial fragment polypeptide selected from the polypeptides of (16) to (19) and partial fragment polypeptides of the polypeptides, and a solid support adhered thereto.

- (22) A polypeptide array, comprising:
- at least one antibody which recognizes a polypeptide or partial fragment polypeptide selected from the polypeptides of (16) to (19) and partial fragment polypeptides of the polypeptides, and a solld support adhered thereto.
- (23) A system based on a computer for identifying a target sequence or a target structure motif derived from a coryneform bacterium, comprising the following:
  - (i) a user input device that inputs at least one nucleotide sequence information selected from SEQ ID NOS:1 to 3501, and target sequence or target structure motif information;
  - (ii) a data storage device for at least temporarily storing the input information;
  - (iii) a comparator that compares the at least one nucleotide sequence information selected from SEQ ID NOS: 1 to 3501 with the target sequence or target structure motif information, recorded by the data storage devic for screening and analyzing nucleotide sequence information which is coincident with or analogous to the target sequence or target structure motif information; and
  - (iv) an output device that shows a screening or analyzing result obtained by the comparator.
  - (24) A method based on a computer for identifying a target sequence or a target structure motif derived from a coryneform bacterium, comprising the following:
    - (i) inputting at least one nucleotide sequence information selected from SEQ ID NOS:1 to 3501, target sequence information or target structure motif information into a user input device;
    - (ii) at least temporarily storing said information;
    - (iii) comparing the at least one nucleotide sequence information selected from SEQ ID NOS:1 to 3501 with the target sequence or target structure motif information; and
    - (iv) screening and analyzing nucleotide sequence information which is coincident with or analogous to the target sequence or target structure motif information.
  - (25) A system based on a computer for identifying a target sequence or a target structure motif derived from a coryneform bacterium, comprising the following:
    - (i) a user input device that inputs at least one amino acid sequence information selected from SEQ ID NOS: 3502 to 7001, and target sequence or target structure motif information;
    - (ii) a data storage device for at least temporarily storing the input information;
    - (iii) a comparator that compares the at least one amino acid sequence information selected from SEQ ID NOS: 3502 to 7001 with the target sequence or target structure motif information, recorded by the data storage device for screening and analyzing amino acid sequence information which is coincident with or analogous to the target sequence or target structure motif information; and
    - (iv) an output device that shows a screening or analyzing result obtained by the comparator.
- (26) A method based on a computer for identifying a target sequence or a target structure motif derived from a coryneform bacterium, comprising the following:
  - (i) inputting at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001, and target sequence information or target structure motif information into a user input d  $\,$  vic  $\,$ ;

- (ii) at least temporarily storing said information;
- (iii) comparing the at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001 with the target sequence or target structure motif information; and
- (iv) screening and analyzing amino acid sequence information which is coincident with or analogous to the target sequence or target structure motif information.
- (27) A system based on a computer for determining a function of a polypeptide encoded by a polynucleotide having a target nucleotide sequence derived from a coryneform bacterium, comprising the following:
  - (i) a user input device that inputs at least one nucleotide sequence information selected from SEQ ID NOS:2 to 3501, function information of a polypeptide encoded by the nucleotide sequence, and target nucleotide sequence information;
  - (ii) a data storage device for at least temporarily storing the input information;
  - (iii) a comparator that compares the at least one nucleotide sequence information selected from SEQ ID NOS: 2 to 3501 with the target nucleotide sequence information, and determining a function of a polypeptide encoded by a polynucleotide having the target nucleotide sequence which is coincident with or analogous to the polynucleotide having at least one nucleotide sequence selected from SEQ ID NOS:2 to 3501; and
  - (iv) an output devices that shows a function obtained by the comparator.
- (28) A method based on a computer for determining a function of a polypeptide encoded by a polypeptide encoded by a polynucleotide having a target nucleotide sequence derived from a coryneform bacterium, comprising the following:
  - (i) inputting at least one nucleotide sequence information selected from SEQ ID NOS:2 to 3501, function information of a polypeptide encoded by the nucleotide sequence, and target nucleotide sequence information; (ii) at least temporarily storing said information;
  - (iii) comparing the at least one nucleotide sequence information selected from SEQ ID NOS:2 to 3501 with the target nucleotide sequence information; and
  - (iv) determining a function of a polypeptide encoded by a polynucleotide having the target nucleotide sequence which is coincident with or analogous to the polynucleotide having at least one nucleotide sequence selected from SEQ ID NOS:2 to 3501.
- (29) A system based on a computer for determining a function of a polypeptide having a target amino acid sequence derived from a coryneform bacterium, comprising the following:
  - (i) a user input device that inputs at least one amino acid sequence information selected from SEQ ID NOS: 3502 to 7001, function information based on the amino acid sequence, and target amino acid sequence information:
  - (ii) a data storing device for at least temporarily storing the input information;
  - (iii) a comparator that compares the at least one amino acid sequence information selected from SEQ ID NOS: 3502 to 7001 with the target amino acid sequence information for determining a function of a polypeptid having the target amino acid sequence which is coincident with or analogous to the polypeptide having at I ast one amino acid sequence selected from SEQ ID NOS:3502 to 7001; and
  - (iv) an output device that shows a function obtained by the comparator.
- (30) A method based on a computer for determining a function of a polypeptide having a target amino acid sequence derived from a coryneform bacterium, comprising the following:
  - (i) inputting at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001, function information based on the amino acid sequence, and target amino acid sequence information;
  - (ii) at least temporarily storing said information;
  - (iii) comparing the at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001 with the target amino acid sequence information; and
  - (iv) determining a function of a polypeptide having the target amino acid sequence which is coincident with or analogous to the polypeptide having at least on amino acid sequence selected from SEQ ID NOS:3502 to 7001.
- (31) The system according to any one of (23), (25), (27) and (29), wherein a coryneform bacterium is a microor-

5

10

15

20

25

30

35

40

45

50

ganism of the genus Corynebacterium, the genus Brevibacterium, or the genus Microbacterium.

(32) The method according to any one of (24), (26), (28) and (30), wherein a coryneform bacterium is a microorganism of the genus Corynebacterium, the genus Brevibacterium, or the genus Microbacterium.

(33) The system according to (31), wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, corynebacterium callunae, corynebacterium herculis, Corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium acetoacidophilum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium ammoniagenes.

(35) A recording medium or storage device which is readable by a computer in which at least one nucleotide sequence information selected from SEQ ID NOS:1 to 3501 or function information based on the nucleotide sequence is recorded, and is usable in the system of (23) or (27) or the method of (24) or (28).

(36) A recording medium or storage device which is readable by a computer in which at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001 or function information based on the amino acid sequence is recorded, and is usable in the system of (25) or (29) or the method of (26) or (30).

(37) The recording medium or storage device according to

(35) or (36), which is a computer readable recording medium selected from the group consisting of a floppy disc, a hard disc, a magnetic tape, a random access memory (RAM), a read only memory (ROM), a magneto-optic disc (MO), CD-ROM, CD-RW, DVD-ROM, DVD-RAM and DVD-RW.

(38) A polypeptide having a homoserine dehydrogenase activity, comprising an amino acid sequence in which the Val residue at the 59th in the amino acid sequence of homoserine dehydrogenase derived from a coryneform bacterium is replaced with an amino acid residue other than a Val residue.

(39) A polypeptide comprising an amino acid sequence in which the Val residue at the 59th position in the amino acid sequence as represented by SEQ ID NO:6952 is replaced with an amino acid residue other than a Val residue. (40) The polypeptide according to (38) or (39), wherein the Val residue at the 59th position is replaced with an Ala residue.

(41) A polypeptide having pyruvate carboxylase activity, comprising an amino acid sequence in which the Pro residue at the 458th position in the amino acid sequence of pyruvate carboxylase derived from a coryneform bacterium is replaced with an amino acid residue other than a Pro residue.

(42) A polypeptide comprising an amino acid sequence in which the Pro residue at the 458th position in the amino acid sequence represented by SEQ ID NO:4265 is replaced with an amino acid residue other than a Pro residue.

(43) The polypeptide according to (41) or (42), wherein the Pro residue at the 458th position is replaced with a Ser residue.

(44) The polypeptide according to any one of (38) to (43), which is derived from Corynebacterium glutamicum.

(45) A DNA encoding the polypeptide of any one of (38) to (44).

(46) A recombinant DNA comprising the DNA of (45).

(47) A transformant comprising the recombinant DNA of (46).

(48) A transformant comprising in its chromosome the DNA of (45).

(49) The transformant according to (47) or (48), which is derived from a coryneform bacterium.

(50) The transformant according to (49), which is derived from Corynebacterium glutamicum.

(51) A method for producing L-lysine, comprising:

culturing the transformant of any one of (47) to (50) in a medium to produce and accumulate L-lysine in the medium, and

recovering the L-lysine from the culture.

(52) A method for breeding a coryneform bacterium using the nucleotide sequence information represented by SEQ ID NOS:1 to 3431, comprising the following:

(i) comparing a nucleotide sequence of a genome or gene of a production strain derived a coryneform bacterium which has been subjected to mutation breeding so as to produce at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogous thereof by a fermentation meth d, with a corresponding nucleotide sequence in SEQ ID NOS:1 to 3431;

(ii) identifying a mutation point present in the production strain based on a result obtained by (i);

(iii) introducing the mutation point into a coryneform bacterium which is free of the mutation point; and

(iv) examining productivity by the fermentation method of the compound selected in (i) of the coryneform

15

20

25

30

35

40

45

50

bact rium obtained in (iii).

5

10

15

20

25

30

35

40

45

50

55

- (53) The method according to (52), wherein the gene is a gene encoding an enzyme in a biosynthetic pathway or a signal transmission pathway.
- (54) The method according to (52), wherein the mutation point is a mutation point relating to a useful mutation which improves or stabilizes the productivity.
- (55) A method for breading a coryneform bacterium using the nucleotide sequence information represented by SEQ ID NOS:1 to 3431, comprising:
  - (i) comparing a nucleotide sequence of a genome or gene of a production strain derived a coryneform bacterium which has been subjected to mutation breeding so as to produce at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogous thereof by a fermentation method, with a corresponding nucleotide sequence in SEQ ID NOS:1 to 3431;
  - (ii) identifying a mutation point present in the production strain based on a result obtain by (i);
  - (iii) deleting a mutation point from a coryneform bacterium having the mutation point; and
  - (iv) examining productivity by the fermentation method of the compound selected in (i) of the coryneform bacterium obtained in (iii).
- (56) The method according to (55), wherein the gene is a gene encoding an en∠yme in a biosynthetic pathway or a signal transmission pathway.
- (57) The method according to (55), wherein the mutation point is a mutation point which decreases or destabilizes the productivity.
- (58) A method for breeding a coryneform bacterium using the nucleotide sequence information represented by SEQ ID NOS:2 to 3431, comprising the following:
  - (i) identifying an isozyme relating to biosynthesis of at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogous thereof, based on the nucleotide sequence information represented by SEQ ID NOS:2 to 3431;
  - (ii) classifying the isozyme identified in (i) into an isozyme having the same activity;
  - (iii) mutating all genes encoding the isozyme having the same activity simultaneously; and
  - (iv) examining productivity by a fermentation method of the compound selected in (i) of the coryneform bacterium which have been transformed with the gene obtained in (iii).
- (59) A method for breeding a coryneform bacterium using the nucleotide sequence information represented by SEQ ID NOS:2 to 3431, comprising the following:
  - (i) arranging a function information of an open reading frame (ORF) represented by SEQ ID NOS:2 to 3431;
  - (ii) allowing the arranged ORF to correspond to an enzyme on a known biosynthesis or signal transmission pathway;
  - (iii) explicating an unknown biosynthesis pathway or signal transmission pathway of a coryneform bacterium in combination with information relating known biosynthesis pathway or signal transmission pathway of a coryneform bacterium;
  - (iv) comparing the pathway explicated in (iii) with a biosynthesis pathway of a target useful product; and
  - (v) transgenetically varying a coryneform bacterium based on the nucleotide sequence information to eith r strengthen a pathway which is judged to be important in the biosynthesis of the target useful product in (iv) or weaken a pathway which is judged not to be important in the biosynthesis of the target useful product in (iv).
- (60) A coryneform bacterium, bred by the method of any one of (52) to (59).
- (61) The coryneform bacterium according to (60), which is a microorganism belonging to the genus *Corynebacterium*, the genus *Brevibacterium*, or the genus *Microbacterium*.
- (62) The coryneform bacterium according to (61), wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium ammoniagenes.
- (63) A method for producing at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an rganic acid and an analogue thereof, comprising:

culturing a coryneform bacterium of any one of (60) to (62) in a medium to produce and accumulate at I ast

one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof;

recovering the compound from the culture.

- (64) The method according to (63), wherein the compound is L-lysine.
- (65) A method for identifying a protein relating to useful mutation based on proteome analysis, comprising the following:
  - (i) preparing

5

10

15

20

25

30

a protein derived from a bacterium of a production strain of a coryneform bacterium which has been subjected to mutation breeding by a fermentation process so as to produce at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof, and a protein derived from a bacterium of a parent strain of the production strain;

- (ii) separating the proteins prepared in (i) by two dimensional electrophoresis;
- (iii) detecting the separated proteins, and comparing an expression amount of the protein derived from the production strain with that derived from the parent strain;
- (iv) treating the protein showing different expression amounts as a result of the comparison with a peptidase to extract peptide fragments;
- (v) analyzing amino acid sequences of the peptide fragments obtained in (iv); and
- (vi) comparing the amino acid sequences obtained in (v) with the amino acid sequence represented by SEQ ID NOS:3502 to 7001 to identifying the protein having the amino acid sequences.

As used herein, the term "proteome", which is a coined word by combining "protein" with "genome", refers to a method for examining of a gene at the polypeptide level.

- (66) The method according to (65), wherein the coryneform bacterium is a microorganism belonging to the genus Corynebacterium, the genus Brevibacterium, or the genus Microbacterium.
- (67) The method according to (66), wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, corynebacterium herculis, Corynebacterium lilium Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium ammoniagenes.
- (68) A biologically pure culture of Corynebacterium glutamicum AHP-3 (FERM BP-7382).
- [0018] The present invention will be described below in more detail, based on the determination of the full nucleotid 35 sequence of coryneform bacteria.
  - 1. Determination of full nucleotide sequence of coryneform bacteria
- 40 [0019] The term "coryneform bacteria" as used herein means a microorganism belonging to the genus Corynebacterium, the genus Brevibacterium or the genus Microbacterium as defined in Bergeys Manual of Determinative Bacteriology, 8: 599 (1974).
- [0020] Examples include Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium glutamicum, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium melas-45 secola, Corynebacterium thermoaminogenes, Brevibacterium saccharolyticum, Brevibacterium immariophilum, Brevibacterium roseum, Brevibacterium thiogenitalis, Microbacterium ammoniaphilum, and the like.
- [0021] Specific examples include Corynebacterium acetoacidophilum ATCC 13870, Corynebacterium acetoglulamicum ATCC 15806, Corynebacterium callunae ATCC 15991, Corynebacterium glutamicum ATCC 13032, Corynebacterium glutamicum ATCC 13060, Corynebacterium glutamicum ATCC 13826 (prior genus and species: Brevibacterium 50 flavum, or Corynebacterium lactofermentum), Corynebacterium glutamicum ATCC 14020 (prior genus and speci s: Brevibacterium divaricatum), Corynebacterium glutamicum ATCC 13869 (prior genus and species: Brevibacterium lactofermentum), Corynebacterium herculis ATCC 13868, Corynebacterium lilium ATCC 15990, Corynebacterium melassecola ATCC 17965, Corynebacterium thermoaminogenes FERM 9244, Brevibacterium saccharolyticum ATCC 14066, Brevibacterium immariophilum ATCC 14068, Brevibacterium roseum ATCC 13825, Brevibacterium thiogenitalis
- 55 ATCC 19240, Microbacterium ammoniaphilum ATCC 15354, and the like.

## (1) Preparation of genome DNA of coryneform bacteria

5

20

25

30

35

40

45

[0022] Coryneform bacteria can be cultured by a conventional method.

Any of a natural medium and a synthetic medium can be used, so long as it is a medium suitable for efficient culturing of the microorganism, and it contains a carbon source, a nitrogen source, an inorganic salt, and the like which can be assimilated by the microorganism.

[0024] In Corynebacterium glutamicum, for example, a BY medium (7 g/l meat extract, 10 g/l peptone, 3 g/l sodium chloride 5 g/l yeast extract, pH 7.2) containing 1% of glycine and the like can be used. The culturing is carried out at 25 to 35°C overnight.

[0025] After the completion of the culture, the cells are recovered from the culture by centrifugation. The resulting cells are washed with a washing solution.

[0026] Examples of the washing solution include STE buffer (10.3% sucrose, 25 mmol/l Tris hydrochloride, 25 mmol/ I ethylenediaminetetraacetic acid (hereinafter referred to as "EDTA"), pH 8.0), and the like.

[0027] Genome DNA can be obtained from the washed cells according to a conventional method for obtaining genome DNA, namely, lysing the cell wall of the cells using a lysozyme and a surfactant (SDS, etc.), eliminating proteins and the like using a phenol solution and a phenol/chloroform solution, and then precipitating the genome DNA with ethanol or the like. Specifically, the following method can be illustrated.

[0028] The washed cells are suspended in a washing solution containing 5 to 20 mg/l lysozyme. After shaking, 5 to 20% SDS is added to lyse the cells. In usual, shaking is gently performed at 25 to 40°C for 30 minutes to 2 hours. After shaking, the suspension is maintained at 60 to 70°C for 5 to 15 minutes for the lysis.

[0029] After the lysis, the suspension is cooled to ordinary temperature, and 5 to 20 ml of Tris-neutralized phenol is added thereto, followed by gently shaking at room temperature for 15 to 45 minutes.

[0030] After shaking, centrifugation (15,000  $\times$  g, 20 minutes, 20°C) is carried out to fractionate the aqueous layer.

[0031] After performing extraction with phenol/chloroform and extraction with chloroform (twice) in the same manner, 3 mol/l sodium acetate solution (pH 5.2) and isopropanol are added to the aqueous layer at 1/10 times volume and 2 times volume, of the aqueous layer, respectively, followed by gently stirring to precipitate the genome DNA.

[0032] The genome DNA is dissolved again in a buffer containing 0.01 to 0.04 mg/ml RNase. As an example of the buffer, TE buffer (10 mmol/l Tris hydrochloride, 1 mol/l EDTA, pH 8.0) can be used. After dissolving, the resultant solution is maintained at 25 to 40°C for 20 to 50 minutes and then extracted successively with phenol, phenol/chloroform and chloroform as in the above case.

[0033] After the extraction, isopropanol precipitation is carried out and the resulting DNA precipitate is washed with 70% ethanol, followed by air drying, and then dissolved in TE buffer to obtain a genome DNA solution.

## (2) Production of shotgun library

[0034] A method for produce a genome DNA library using the genome DNA of the coryneform bacteria prepared in the above (1) include a method described in Molecular Cloning, A laboratory Manual, Second Edition (1989) (hereinafter referred to as "Molecular Cloning, 2nd ed."). In particular, the following method can be exemplified to prepare a genome DNA library appropriately usable in determining the full nucleotide sequence by the shotgun method.

[0035] To 0.01 mg of the genome DNA of the coryneform bacteria prepared in the above (1), a buffer, such as TE buffer or the like, is added to give a total volume of 0.4 ml. Then, the genome DNA is digested into fragments of 1 to 10 kb with a sonicator (Yamato Powersonic Model 50). The treatment with the sonicator is performed at an output of 20 continuously for 5 seconds.

[0036] The resulting genome DNA fragments are blunt-ended using DNA blunting kit (manufactured by Takara Shuzo) or the like.

[0037] The blunt-ended genome fragments are fractionated by agarose gel or polyacrylamide gel electrophoresis and genome fragments of 1 to 2 kb are cut out from the gel.

[0038] To the gel, 0.2 to 0.5 ml of a buffer for eluting DNA, such as MG elution buffer (0.5 mol/l ammonium acetate, 10 mmol/l magnesium acetate, 1 mmol/l EDTA, 0.1% SDS) or the like, is added, followed by shaking at 25 to 40°C overnight to elute DNA.

[0039] The resulting DNA eluate is treated with phenol/chloroform and then precipitated with ethanol to obtain a genome library insert.

[0040] This insert is ligated into a suitable vector, such as pUC18 Smal/SAP (manufactured by Amersham Pharmacia Biotech) or the like, using T4 ligase (manufactured by Takara Shuzo) or the like. The ligation can be carried out by allowing a mixture to stand at 10 to 20°C for 20 to 50 hours.

[0041] The resulting ligation product is precipitated with ethanol and diss lived in 5 t 20 µl of TE buffer.

[0042] Escherichia coli is transformed in accordance with a conventional method using 0.5 to 2 µl of the ligati n solution. Examples of the transformation method include the electroporation method using ELECTRO MAX DHIOB

(manufactur d by Life Technologies) for *Escherichia coli*. The electroporation method can be carried out under the conditions as described in the manufacturer's instructions.

[0043] The transformed *Escherichia coli* is spread on a suitable selection medium containing agar, for example, LB plate medium containing 10 to 100 mg/l ampicillin (LB medium (10 g/l bactotrypton, 5 g/l yeast extract, 10 g/l sodium chloride, pH 7.0) containing 1.6% of agar) when pUC18 is used as the cloning vector, and cultured therein.

[0044] The transformant can be obtained as colonies formed on the plate medium. In this step, it is possible to select the transformant having the recombinant DNA containing the genome DNA as white colonies by adding X-gal and IPTG (isopropyl-β-thiogalactopyranoside) to the plate medium.

[0045] The transformant is allowed to stand for culturing in a 96-well titer plate to which 0.05 ml of the LB medium containing 0.1 mg/ml of ampicillin has been added in each well. The resulting culture can be used in an experiment of (4) described below. Also, the culture solution can be stored at -80°C by adding 0.05 ml per well of the LB medium containing 20% glycerol to the culture solution, followed by mixing, and the stored culture solution can be used at any time.

## (3) Production of cosmid library

10

15

25

45

50

[0046] The genome DNA (0.1 mg) of the coryneform bacteria prepared in the above (1) is partially digested with a restriction enzyme, such as Sau3AI or the like, and then ultracentrifuged (26,000 rpm, 18 hours, 20°C) under a 10 to 40% sucrose density gradient using a 10% sucrose buffer (1 mol/i Nacl, 20 mmol/i Tris hydrochloride, 5 mmol/i EDTA, 10% sucrose, pH 8.0) and a 40% sucrose buffer (elevating the concentration of the 10% sucrose buffer to 40%).

[0047] After the centrifugation, the thus separated solution is fractionated into tubes in 1 ml per each tube. Aft r confirming the DNA fragment size of each fraction by agarose gel electrophoresis, a fraction rich in DNA fragments of about 40 kb is precipitated with ethanol.

[0048] The resulting DNA fragment is ligated to a cosmid vector having a cohesive end which can be ligated to the fragment. When the genome DNA is partially digested with Sau3AI, the partially digested product can be ligated to, for example, the BamHI site of superCos1 (manufactured by Stratagene) in accordance with the manufacture's instructions.

[0049] The resulting ligation product is packaged using a packaging extract which can be prepared by a method described in *Molecular Cloning*, 2nd ed. and then used in transforming *Escherichia coli*. More specifically, the ligation product is packaged using, for example, a commercially available packaging extract, Gigapack III Gold Packaging Extract (manufactured by Stratagene) in accordance with the manufacture's instructions and then introduced into *Escherichia coli* XL-1-BlueMR (manufactured by Stratagene) or the like.

[0050] The thus transformed Escherichia coli is spread on an LB plate medium containing ampicillin, and cultured therein.

35 [0051] The transformant can be obtained as colonies formed on the plate medium.

[0052] The transformant is subjected to standing culture in a 96-well titer plate to which 0.05 ml of the LB medium containing 0.1 mg/ml ampicillin has been added.

[0053] The resulting culture can be employed in an experiment of (4) described below. Also, the culture solution can be stored at -80°C by adding 0.05 ml per well of the LB medium containing 20% glycerol to the culture solution, followed by mixing, and the stored culture solution can be used at any time.

## (4) Determination of nucleotide sequence

## (4-1) Preparation of template

[0054] The full nucleotide sequence of genome DNA of coryneform bacteria can be determined basically according to the whole genome shotgun method (Science, 269: 496-512 (1995)).

[0055] The template used in the whole genome shotgun method can be prepared by PCR using the library prepared in the above (2) (DNA Research, 5: 1-9 (1998)).

[0056] Specifically, the template can be prepared as follows.

[0057] The clone derived from the whole genome shotgun library is inoculated by using a replicator (manufactured by GENETIX) into each well of a 96-well plate to which 0.08 ml per well of the LB medium containing 0.1 mg/ml ampicillin has been added, followed by stationarily culturing at 37°C overnight.

[0058] Next, the culture solution is transported, using a copy plate (manufactured by Tokken), into each well of a 96-well reaction plate (manufactured by PE Biosystems) to which 0.025 ml per well of a PCR reaction solution has been added using TaKaRa Ex Taq (manufactured by Takara Shuzo). Then, PCR is carried out in accordance with the protocol by Makino et al. (DNA Research, 5: 1-9 (1998)) using Gen Amp PCR System 9700 (manufactured by PE Biosystems) to amplify the inserted fragments.

[0059] The excessive primers and nucleotides are eliminated using a kit for purifying a PCR product, and the product is used as the template in the sequencing reaction.

[0060] It is also possible to determine the nucleotide sequence using a double-stranded DNA plasmid as a template.

[0061] The double-stranded DNA plasmid used as the template can be obtained by the following method.

[0062] The clone derived from the whole genome shotgun library is inoculated into each well of a 24- or 96-well plate to which 1.5 ml per well of a  $2 \times YT$  medium (16 g/l bactotrypton, 10 g/l yeast extract, 5 g/l sodium chloride, pH 7.0) containing 0.05 mg/ml ampicillin has been added, followed by culturing under shaking at 37°C overnight.

[0063] The double-stranded DNA plasmid can be prepared from the culture solution using an automatic plasmid preparing machine KURABO PI-50 (manufactured by Kurabo Industries), a multiscreen (manufactured by Millipore) or the like, according to each protocol.

[0064] To purify the plasmid, Biomek 2000 manufactured by Beckman Coulter and the like can be used.

[0065] The resulting purified double-stranded DNA plasmid is dissolved in water to give a concentration of about 0.1 mg/ml. Then, it can be used as the template in sequencing.

## (4-2) Sequencing reaction

10

15

25

35

40

45

50

55

[0066] The sequencing reaction can be carried out according to a commercially available sequence kit or the like. A specific method is exemplified below.

[0067] To 6 μl of a solution of ABI PRISM BigDye Terminator Cycle Sequencing Ready Reaction Kit (manufactured by PE Biosystems), 1 to 2 pmol of an M13 regular direction primer (M13-21) or an M13 reverse direction primer (MI3REV) (DNA Research, 5: 1-9 (1998)) and 50 to 200 ng of the template prepared in the above (4-1) (the PCR product or plasmid) to give 10 μl of a sequencing reaction solution.

[0068] A dye terminator sequencing reaction (35 to 55 cycles) is carried out using this reaction solution and GeneAmp PCR System 9700 (manufactured by PE Biosystems) or the like. The cycle parameter can be determined in accordance with a commercially available kit, for example, the manufacture's instructions attached with ABI PRISM Big Dye T reminator Cycle Sequencing Ready Reaction Kit.

[0069] The sample can be purified using a commercially available product, such as Multi Screen HV plate (manufactured by Millipore) or the like, according to the manufacture's instructions.

[0070] The thus purified reaction product is precipitated with ethanol, dried and then used for the analysis. The dried reaction product can be stored in the dark at -30°C and the stored reaction product can be used at any time.

[0071] The dried reaction product can be analyzed using a commercially available sequencer and an analyzer according to the manufacture's instructions.

[0072] Examples of the commercially available sequencer include ABI PRISM 377 DNA Sequencer (manufactured by PE Biosystems). Example of the analyzer include ABI PRISM 3700 DNA Analyzer (manufactured by PE Biosystems).

#### (5) Assembly

[0073] A software, such as phred (The University of Washington) or the like, can be used as base call for us in analyzing the sequence information obtained in the above (4). A software, such as Cross\_Match (The University of Washington) or SPS Cross\_Match (manufactured by Southwest Parallel Software) or the like, can be used to mask the vector sequence information.

[0074] For the assembly, a software, such as phrap (The University of Washington), SPS phrap (manufactured by Southwest Parallel Software) or the like, can be used.

[0075] In the above, analysis and output of the results thereof, a computer such as UNIX, PC, Macintosh, and the like can be used.

[0076] Contig obtained by the assembly can be analyzed using a graphical editor such as consed (The University of Washington) or the like.

[0077] It is also possible to perform a series of the operations from the base call to the assembly in a lump using a script phredPhrap attached to the consed.

[0078] As used herein, software will be understood to also be referred to as a comparator.

## (6) Determination of nucleotide sequence in gap part

[0079] Each of the cosmids in the cosmid library constructed in the above (3) is prepared in the same manner as in the preparation of the double-stranded DNA plasmid described in the above (4-1). The nucleotide sequence at the independent of the cosmid is determined using a commercially available kit, such as ABI PRISM BigDye Terminator Cycle Sequencing Ready Reaction Kit (manufactured by PE Biosystems) according to the manufacture's instructions.

[0080] About 800 cosmid clon's are sequenced at both ends of the inserted fragment to detect a nucleotide sequence in the contig derived from the shotgun sequencing obtained in (5) which is coincident with the sequence. Thus, the chain linkage between respective cosmid clones and respective contigs are clarified, and mutual alignment is carried out. Furthermore, the results are compared with known physical maps to map the cosmids and the contigs. In case of Corynebacterium glutamicum ATCC 13032, a physical map of Mol. Gen. Genet., 252: 255-265 (1996) can be used.

[0081] The sequence in the region which cannot be covered with the contigs (gap part) can be determined by the following method.

[0082] Clones containing sequences positioned at the ends of the contigs are selected. Among these, a clone wherein only one end of the inserted fragment has been determined is selected and the sequence at the opposite end of the inserted fragment is determined.

[0083] A shotgun library clone or a cosmid clone derived therefrom containing the sequences at the respective ends of the inserted fragments in the two contigs is identified and the full nucleotide sequence of the inserted fragment of the clone is determined.

[0084] According to this method, the nucleotide sequence of the gap part can be determined.

[0085] When no shotgun library clone or cosmid clone covering the gap part is available, primers complementary to the end sequences of the two different contigs are prepared and the DNA fragment in the gap part is amplified. Then, sequencing is performed by the primer walking method using the amplified DNA fragment as a template or by the shotgun method in which the sequence of a shotgun clone prepared from the amplified DNA fragment is determined. Thus, the nucleotide sequence of the above-described region can be determined.

[0086] In a region showing a low sequence accuracy, primers are synthesized using AUTOFINISH function and NAVIGATING function of consed (The University of Washington), and the sequence is determined by the primer walking method to improve the sequence accuracy.

[0087] Examples of the thus determined nucleotide sequence of the full genome include the full nucleotide sequence of genome of *Corynobacterium glutamicum* ATCC 13032 represented by SEQ ID NO:1.

(7) Determination of nucleotide sequence of microorganism genome DNA using the nucleotide sequence represented by SEQ ID NO:1

[0088] A nucleotide sequence of a polynucleotide having a homology of 80% or more with the full nucleotide sequence of Corynebacterium glutamicum ATCC 13032 represented by SEQ ID NO:1 as determined above can also be determined using the nucleotide sequence represented by SEQ ID NO:1, and the polynucleotide having a nucleotid s quence having a homology of 80% or more with the nucleotide sequence represented by SEQ ID NO:1 of the present invention is within the scope of the present invention. The term "polynucleotide having a nucleotide sequence having a homology of 80% or more with the nucleotide sequence represented by SEQ ID NO:1 of the present invention\* is a polynucleotide in which a full nucleotide sequence of the chromosome DNA can be determined using as a prim r an oligonucleotide composed of continuous 5 to 50 nucleotides in the nucleotide sequence represented by SEQ ID NO: 1, for example, according to PCR using the chromosome DNA as a template. A particularly preferred primer in determination of the full nucleotide sequence is an oligonucleotide having nucleotide sequences which are position d at the interval of about 300 to 500 bp, and among such oligonucleotides, an oligonucleotide having a nucleotide sequence selected from DNAs encoding a protein relating to a main metabolic pathway is particularly preferred. The polynucleotide in which the full nucleotide sequence of the chromosome DNA can be determined using the oligonucleotid includes polynucleotides constituting a chromosome DNA derived from a microorganism belonging to coryneform bacteria. Such a polynucleotide is preferably a polynucleotide constituting chromosome DNA derived from a microorganism belonging to the genus Corynebacterium, more preferably a polynucleotide constituting a chromosome DNA of Corynebacterium glutamicum.

2. Identification of ORF (open reading frame) and expression regulatory fragment and determination of the function of ORF

[0089] Based on the full nucleotide sequence data of the genome derived from coryneform bacteria determined in the above item 1, an ORF and an expression modulating fragment can be identified. Furthermore, the function of th thus determined ORF can be determined.

[0090] The ORF means a continuous region in the nucleotide sequence of mRNA which can be translated as an amino acid sequence to mature to a protein. A region of the DNA coding for the ORF of mRNA is also called ORF.

[0091] The expressi n modulating fragment (hereinafter r ferred to as "EMF") is used herein to define a series of polynucleotide fragments which modulate the expression of the ORF or another sequence ligated operatably thereto. The expression "modulate the expression of a sequence ligated operatably" is used herein to refer t changes in the expression of a sequence due to the presence of the EMF. Examples of the EMF include a promot r, an operator, an

20

25

30

35

40

45

enhanc r, a silencer, a ribosome-binding sequence, a transcriptional termination sequence, and the like. In coryneform bacteria, an EMF is usually present in an intergenic segment (a fragment positioned between two genes; about 10 to 200 nucleotides in length). Accordingly, an EMF is frequently present in an intergenic segment of 10 nucleotides or longer. It is also possible to determine or discover the presence of an EMF by using known EMF sequences as a target sequence or a target structural motif (or a target motif) using an appropriate software or comparator, such as FASTA (*Proc. Natl. Acad. Sci. USA, 85*: 2444-48 (1988)), BLAST (*J. Mol. Biol., 215*: 403-410 (1990)) or the like. Also, it can be identified and evaluated using a known EMF-capturing vector (for example, pKK232-8; manufactured by Amersham Pharmacia Biotech).

[0092] The term "target sequence" is used herein to refer to a nucleotide sequence composed of 6 or more nucleotides, an amino acid sequence composed of 2 or more amino acids, or a nucleotide sequence encoding this amino acid sequence composed of 2 or more amino acids. A longer target sequence appears at random in a data base at the lower possibility. The target sequence is preferably about 10 to 100 amino acid residues or about 30 to 300 nucleotide residues.

10

15

20

25

30

35

40

50

55

[0093] The term "target structural motif" or "target motif" is used herein to refer to a sequence or a combination of sequences selected optionally and reasonably. Such a motif is selected on the basis of the threedimensional structure formed by the folding of a polypeptide by means known to one of ordinary skill in the art. Various motives are known.

[0094] Examples of the target motif of a polypeptide include, but are not limited to, an enzyme activity site, a protein-protein interaction site, a signal sequence, and the like. Examples of the target motif of a nucleic acid include a promoter sequence, a transcriptional regulatory factor binding sequence, a hair pin structure, and the like.

[0095] Examples of highly useful EMF include a high-expression promoter, an inducible-expression promoter, and the like. Such an EMF can be obtained by positionally determining the nucleotide sequence of a gene which is known or expected as achieving high expression (for example, ribosomal RNA gene: GenBank Accession No. M16175 r Z46753) or a gene showing a desired induction pattern (for example, isocitrate lyase gene induced by acetic acid: Japanese Published Unexamined Patent Application No. 56782/93) via the alignment with the full genome nucleotide sequence determined in the above item 1, and isolating the genome fragment in the upstream part (usually 200 to 500 nucleotides from the translation initiation site). It is also possible to obtain a highly useful EMF by selecting an EMF showing a high expression efficiency or a desired induction pattern from among promoters captured by the EMF-capturing vector as described above.

[0096] The ORF can be identified by extracting characteristics common to individual ORFs, constructing a general model based on these characteristics, and measuring the conformity of the subject sequence with the model. In the identification, a software, such as GeneMark (*Nuc. Acids. Res., 22*: 4756-67 (1994): manufactured by GenePro)), GeneMark.hmm (manufactured by GenePro), GeneHacker (*Protein, Nucleic Acid and Enzyme, 42*: 3001-07 (1997)), Glimmer (*Nuc. Acids. Res., 26*: 544-548 (1998): manufactured by The Institute of Genomic Research), or the like, can be used. In using the software, the default (initial setting) parameters are usually used, though the parameters can be optionally changed.

[0097] In the above-described comparisons, a computer, such as UNIX, PC, Macintosh, or the like, can be used.
[0098] Examples of the ORF determined by the method of the present invention include ORFs having the nucleotide sequences represented by SEQ ID NOS:2 to 3501 present in the genome of *Corynebacterium glutamicum* as represented by SEQ ID NO:1. In these ORFs, polypeptides having the amino acid sequences represented by SEQ ID NOS: 3502 to 7001 are encoded.

[0099] The function of an ORF can be determined by comparing the identified amino acid sequence of the ORF with known homologous sequences using a homology searching software or comparator, such as BLAST, FAST, Smith & Waterman (*Meth. Enzym., 164*: 765 (1988)) or the like on an amino acid data base, such as Swith-Prot, PIR, GenBank-nr-aa, GenPept constituted by protein-encoding domains derived from GenBank data base, OWL or the like.

[0100] Furthermore, by the homology searching, the identity and similarity with the amino acid sequences of known proteins can also be analyzed.

[0101] With respect of the term "identity" used herein, where two polypeptides each having 10 amino acids are different in the positions of 3 amino acids, these polypeptides have an identity of 70% with each other. In case wherein one of the different 3 amino acids is analogue (for example, leucine and isoleucine), these polypeptides have a similarity f 80%.

[0102] As a specific example, Table 1 shows the registration numbers in known data bases of sequences which are judged as having the highest similarity with the nucleotide sequence of the ORF derived from Corynebacterium glutamicum ATCC 13032, genes of these sequences, functions of these genes, and identities thereof compared with known amino acid translation sequences.

[0103] Thus, a great number of novel genes deriv d from coryneform bacteria can be identified by det mining the full nucleotide sequence of the genome derived from coryneform bacterium by the means of the present invintion. M reover, the function of the proteins encoded by these genes can be determined. Since coryneform bacteria are industrially highly useful microorganisms, many of the identified genes are industrially useful.

[0104] Moreov r, the characteristics of respective microorganisms can be clarified by classifying the functions thus determined. As a result, valuable information in breeding is obtained.

[0105] Furthermore, from the ORF information derived from coryneform bacteria, the ORF corresponding to the microorganism is prepared and obtained according to the general method as disclosed in *Molecular Cloning*, 2nd ed. or the like. Specifically, an oligonucleotide having a nucleotide sequence adjacent to the ORF is synthesized, and the ORF can be isolated and obtained using the oligonucleotide as a primer and a chromosome DNA derived from coryneform bacteria as a template according to the general PCR cloning technique. Thus obtained ORF sequences include polynucleotides comprising the nucleotide sequence represented by any one of SEQ ID NOS:2 to 3501.

[0106] The ORF or primer can be prepared using a polypeptide synthesizer based on the above sequence information.

[0107] Examples of the polynucleotide of the present invention include a polynucleotide containing the nucleotide sequence of the ORF obtained in the above, and a polynucleotide which hybridizes with the polynucleotide under stringent conditions.

[0108] The polynucleotide of the present invention can be a single-stranded DNA, a double-stranded DNA and a single-stranded RNA, though it is not limited thereto.

[0109] The polynucleotide which hybridizes with the polynucleotide containing the nucleotide sequence of the ORF obtained in the above under stringent conditions includes a degenerated mutant of the ORF. A degenerated mutant is a polynucleotide fragment having a nucleotide sequence which is different from the sequence of the ORF of the present invention which encodes the same amino acid sequence by degeneracy of a gene code.

[0110] Specific examples include a polynucleotide comprising the nucleotide sequence represented by any one of SEQ ID NOS:2 to 3431, and a polynucleotide which hybridizes with the polynucleotide under stringent conditions.

[0111] A polynucleotide which hybridizes under stringent conditions is a polynucleotide obtained by colony hybridization, plaque hybridization, Southern blot hybridization or the like using, as a probe, the polynucleotide having th nucleotide sequence of the ORF identified in the above. Specific examples include a polynucleotide which can be identified by carrying out hybridization at 65°C in the presence of 0.7-1.0 M NaCl using a filter on which a polynucleotide prepared from colonies or plaques is immobilized, and then washing the filter with 0.1x to 2x SSC solution (the composition of lx SSC contains 150 mM sodium chloride and 15 mM sodium citrate) at 65°C.

[0112] The hybridization can be carried out in accordance with known methods described in, for example, *Molecular Cloning*, 2nd ed., *Current Protocols in Molecular Biology, DNA Cloning 1: Core Techniques, A Practical Approach*, Second Edition, Oxford University (1995) or the like. Specific examples of the polynucleotide which can be hybridized include a DNA having a homology of 60% or more, preferably 80% or more, and particularly preferably 95% or more, with the nucleotide sequence represented by any one of SEQ ID NO:2 to 3431 when calculated using default (initial setting) parameters of a homology searching software, such as BLAST, FASTA, Smith-Waterman or the like.

[0113] Also, the polynucleotide of the present invention includes a polynucleotide encoding a polypeptide comprising the amino acid sequence represented by any one of SEQ ID NOS:3502 to 6931 and a polynucleotide which hybridizes with the polynucleotide under stringent conditions.

[0114] Furthermore, the polynucleotide of the present invention includes a polynucleotide which is present in the 5' upstream or 3' downstream region of a polynucleotide comprising the nucleotide sequence of any one of SEQ ID NOS: 2 to 3431 in a polynucleotide comprising the nucleotide sequence represented by SEQ ID NO:1, and has an activity of regulating an expression of a polypeptide encoded by the polynucleotide. Specific examples of the polynucleotid having an activity of regulating an expression of a polypeptide encoded by the polynucleotide includes a polynucleotide encoding the above described EMF, such as a promoter, an operator, an enhancer, a silencer, a ribosome-binding sequence, a transcriptional termination sequence, and the like.

[0115] The primer used for obtaining the ORF according to the above PCR cloning technique includes an oligonucleotide comprising a sequence which is the same as a sequence of 10 to 200 continuous nucleotides in the nucleotid sequence of the ORF and an adjacent region or an oligonucleotide comprising a sequence which is complementary to the oligonucleotide. Specific examples include an oligonucleotide comprising a sequence which is the same as a sequence of 10 to 200 continuous nucleotides of the nucleotide sequence represented by any one of SEQ ID NOS:1 to 3431, and an oligonucleotide comprising a sequence of at least 10 to 20 continuous nucleotide of any one of SEQ ID NOS:1 to 3431. When the primers are used as a sense primer and an antisense primer, the above-described oligonucleotides in which melting temperature (T<sub>m</sub>) and the number of nucleotides are not significantly different from each other are preferred.

[0116] The oligonucleotide of the present invention includes an oligonucleotide comprising a sequence which is th same as 10 to 200 continuous nucleotides of the nucleotide sequence represented by any one of SEQ ID NOS:1 to 3431 or an oligonucleotide comprising a sequence c mplementary to the oligonucleotide.

[0117] Also, analogues of these oligonucleotides (hereinafter also referred to as "analogous oligonucleotides") are also provided by the present invention and are useful in the methods described herein.

[0118] Examples of the analogous oligonucleotides include analogous oligonucleotides in which a phosphodiester

10

20

30

40

50

bond in an oligonucleotide is convirted to a phosphorothioat bond, analogous oligonucleotides in which a phosphodister bond in an oligonucleotide is converted to an N3'-P5' phosphoamidate bond, analogous oligonucleotides in which ribose and a phosphodiester bond in an oligonucleotide is converted to a peptide nucleic acid bond, analogous oligonucleotides in which uracil in an oligonucleotide is replaced with C-5 propynyluracil, analogous oligonucleotides in which uracil in an oligonucleotide is replaced with C-5 thiazoluracil, analogous oligonucleotides in which cytosine in an oligonucleotide is replaced with C-5 propynylcytosine, analogous oligonucleotides in which cytosine in an oligonucleotide is replaced with phenoxazine-modified cytosine, analogous oligonucleotides in which ribose in an oligonucleotide is replaced with 2'-O-propylribose, analogous oligonucleotides in which ribose in an oligonucleotide with 2'-methoxyethoxyribose, and the like (*Cell Engineering*, 16: 1463 (1997)).

[0119] The above oligonucleotides and analogous oligonucleotides of the present invention can be used as probes for hybridization and antisense nucleic acids described below in addition to as primers.

[0120] Examples of a primer for the antisense nucleic acid techniques known in the art include an oligonucleotide which hybridizes the oligonucleotide of the present invention under stringent conditions and has an activity regulating expression of the polypeptide encoded by the polynucleotide, in addition to the above oligonucleotide.

## 3. Determination of isozymes

5

10

15

20

25

30

35

40

45

50

[0121] Many mutants of coryneform bacteria which are useful in the production of useful substances, such as amino acids, nucleic acids, vitamins, saccharides, organic acids, and the like, are obtained by the present invention.

[0122] However, since the gene sequence data of the microorganism has been, to date, insufficient, useful mutants have been obtained by mutagenic techniques using a mutagen, such as nitrosoguanidine (NTG) or the like.

[0123] Although genes can be mutated randomly by the mutagenic method using the above-described mutagen, all genes encoding respective isozymes having similar properties relating to the metabolism of intermediates cannot be mutated. In the mutagenic method using a mutagen, genes are mutated randomly. Accordingly, harmful mutati ns worsening culture characteristics, such as delay in growth, accelerated foaming, and the like, might be imparted at a great frequency, in a random manner.

[0124] However, if gene sequence information is available, such as is provided by the present invention, it is possible to mutate all of the genes encoding target isozymes. In this case, harmful mutations may be avoided and the target mutation can be incorporated.

[0125] Namely, an accurate number and sequence information of the target isozymes in coryneform bacteria can be obtained based on the ORF data obtained in the above item 2. By using the sequence information, all of the target isozyme genes can be mutated into genes having the desired properties by, for example, the site-specific mutagenesis method described in *Molecular Cloning*, 2nd ed. to obtain useful mutants having elevated productivity of useful substances.

4. Clarification or determination of biosynthesis pathway and signal transmission pathway

[0126] Attempts have been made to elucidate biosynthesis pathways and signal transmission pathways in a number of organisms, and many findings have been reported. However, there are many unknown aspects of coryneform bacteria since a number of genes have not been identified so far.

[0127] These unknown points can be clarified by the following method.

[0128] The functional information of ORF derived from coryneform bacteria as identified by the method of above it m 2 is arranged. The term "arranged" means that the ORF is classified based on the biosynthesis pathway of a substance or the signal transmission pathway to which the ORF belongs using known information according to the functional information. Next, the arranged ORF sequence information is compared with enzymes on the biosynthesis pathways or signal transmission pathways of other known organisms. The resulting information is combined with known data on coryneform bacteria. Thus, the biosynthesis pathways and signal transmission pathways in coryneform bacteria, which have been unknown so far, can be determined.

[0129] As a result that these pathways which have been unknown or unclear hitherto are clarified, a useful mutant for producing a target useful substance can be efficiently obtained.

[0130] When the thus clarified pathway is judged as important in the synthesis of a useful product, a useful mutant can be obtained by selecting a mutant wherein this pathway has been strengthened. Also, when the thus clarified pathway is judged as not important in the biosynthesis of the target useful product, a useful mutant can be obtained by selecting a mutant wherein the utilization frequency of this pathway is lowered.

5. Clarification or determination of useful mutation point

[0131] Many useful mutants of coryneform bacteria which are suitable for the production of useful substances, such

16

as amino acids, nucleic acids, vitamins, saccharides, organic acids, and the like, have be no obtained. However, it is hardly known which mutation point is imparted to a gene to improve the productivity.

[0132] However, mutation points contained in production strains can be identified by comparing desired sequences of the genome DNA of the production strains obtained from coryneform bacteria by the mutagenic technique with the nucleotide sequences of the corresponding genome DNA and ORF derived from coryneform bacteria determined by the methods of the above items 1 and 2 and analyzing them

[0133] Moreover, effective mutation points contributing to the production can be easily specified from among these mutation points on the basis of known information relating to the metabolic pathways, the metabolic regulatory mechanisms, the structure activity correlation of enzymes, and the like.

[0134] When any efficient mutation can be hardly specified based on known data, the mutation points thus identified can be introduced into a wild strain of coryneform bacteria or a production strain free of the mutation. Then, it is examined whether or not any positive effect can be achieved on the production.

[0135] For example, by comparing the nucleotide sequence of homoserine dehydrogenase gene hom of a lysine-producing B-6 strain of Corynebacterium glutamicum (Appl. Microbiol. Biotechnol., 32: 269-273 (1989)) with the nucleotide sequence corresponding to the genome of Corynebacterium glutamicum ATCC 13032 according to the present invention, a mutation of amino acid replacement in which valine at the 59-position is replaced with alanine (Val59Ala) was identified. A strain obtained by introducing this mutation into the ATCC 13032 strain by the gene replacement method can produce lysine, which indicates that this mutation is an effective mutation contributing to the production of lysine.

[0136] Similarly, by comparing the nucleotide sequence of pyruvate carboxylase gene pyc of the B-6 strain with the nucleotide sequence corresponding to the ATCC 13032 genome, a mutation of amino acid replacement in which proline at the 458-position was replaced with serine (Pro458Ser) was identified. A strain obtained by introducing this mutation into a lysine-producing strain of No. 58 (FERM BP-7134) of Corynebacterium glutamicum free of this mutation shows an improved lysine productivity in comparison with the No. 58 strain, which indicates that this mutation is an effective mutation contributing to the production of lysine.

[0137] In addition, a mutation A1a213Thr in glucose-6-phosphate dehydrogenase was specified as an effective mutation relating to the production of lysine by detecting glucose-6-phosphate dehydrogenase gene zwf of the B-6 strain.

[0138] Furthermore, the lysine-productivity of Corynebacterium glutamicum was improved by replacing the base at the 932-position of aspartokinase gene lysC of the Corynebacterium glutamicum ATCC 13032 genome with cytosine to thereby replace threonine at the 311-position by isoleucine, which indicates that this mutation is an effective mutation contributing to the production of lysine.

[0139] Also, as another method to examine whether or not the identified mutation point is an effective mutation, ther is a method in which the mutation possessed by the lysine-producing strain is returned to the sequence of a wild type strain by the gene replacement method and whether or not it has a negative influence on the lysine productivity. For example, when the amino acid replacement mutation Val59Ala possessed by *hom* of the lysine-producing B-6 strain was returned to a wild type amino acid sequence, the lysine productivity was lowered in comparison with the B-6 strain. Thus, it was found that this mutation is an effective mutation contributing to the production of lysine.

[0140] Effective mutation points can be more efficiently and comprehensively extracted by combining, if needed, the DNA array analysis or proteome analysis described below.

6. Method of breeding industrially advantageous production strain

[0141] It has been a general practice to construct production strains, which are used industrially in the fermentation production of the target useful substances, such as amino acids, nucleic acids, vitamins, saccharides, organic acids, and the like, by repeating mutagenesis and breeding based on random mutagenesis using mutagens, such as NTG or the like, and screening.

[0142] In recent years, many examples of improved production strains have been made through the use of recombinant DNA techniques. In breeding, however, most of the parent production strains to be improved are mutants obtained by a conventional mutagenic procedure (W. Leuchtenberger, *Amino Acids - Technical Production and Use.* In: Roehr (ed) Biotechnology, second edition, vol. 6, products of primary metabolism. VCH Verlagsgesellschaft mbH, Weinheim, P 465 (1996)).

[0143] Although mutagenesis methods have largely contributed to the progress of the fermentation industry, they suffer from a serious problem of multiple, random introduction of mutations into every part of the chromosome. Since many mutations are accumulated in a single chromosome each time a strain is improved, a production strain obtained by the random mutation and selecting is generally inferior in properties (for example, showing poor growth, delayed consumption of saccharides, and poor resistance to stresses such as temperature and oxygen) to a wild type strain, which brings about troubles such as failing to establish a sufficiently elevated productivity, being frequently contaminated with miscellaneous bacteria, requiring troublesome procedures in culture maintenance, and the like, and, in its

20

25

30

40

45

50

turn, levating the production cost in practice. In addition, the improvement in the productivity is based on random mutations and thus the mechanism thereof is unclear. Therefore, it is very difficult to plan a rational breeding strategy for the subsequent improvement in the productivity.

**[0144]** According to the present invention, effective mutation points contributing to the production can be fliciently specified from among many mutation points accumulated in the chromosome of a production strain which has been bred from coryneform bacteria and, therefore, a novel breeding method of assembling these effective mutations in the coryneform bacteria can be established. Thus, a useful production strain can be reconstructed. It is also possible to construct a useful production strain from a wild type strain.

[0145] Specifically, a useful mutant can be constructed in the following manner.

[0146] One of the mutation points is incorporated into a wild type strain of coryneform bacteria. Then, it is examined whether or not a positive effect is established on the production. When a positive effect is obtained, the mutation point is saved. When no effect is obtained, the mutation point is removed. Subsequently, only a strain having the effective mutation point is used as the parent strain, and the same procedure is repeated. In general, the effectiveness of a mutation positioned upstream cannot be clearly evaluated in some cases when there is a rate-determining point in the downstream of a biosynthesis pathway. It is therefore preferred to successively evaluate mutation points upward from downstream.

[0147] By reconstituting effective mutations by the method as described above in a wild type strain or a strain which has a high growth speed or the same ability to consume saccharides as the wild type strain, it is possible to construct an industrially advantageous strain which is free of troubles in the previous methods as described above and to conduct fermentation production using such strains within a short time or at a higher temperature.

[0148] For example, a lysine-producing mutant B-6 (Appl. Microbiol. Biotechnol., 32: 262-273 (1989)), which is obtained by multiple rounds of random mutagenesis from a wild type strain Corynebacterium glutamicum ATCC 13032, enables lysine fermentation to be performed at a temperature between 30 and 34°C but shows lowered growth and lysine productivity at a temperature exceeding 34°C. Therefore, the fermentation temperature should be maintained at 34°C or lower. In contrast thereto, the production strain described in the above item 5, which is obtained by rec n-stituting effective mutations relating to lysine production, can achieve a productivity at 40 to 42°C equal or superior to the result obtained by culturing at 30 to 34°C. Therefore, this strain is industrially advantageous since it can save the load of cooling during the fermentation.

[0149] When culture should be carried out at a high temperature exceeding 43°C, a production strain capable of conducting fermentation production at a high temperature exceeding 43°C can be obtained by reconstituting us ful mutations in a microorganism belonging to the genus *Corynebacterium* which can grow at high temperature exceeding 43°C. Examples of the microorganism capable of growing at a high temperature exceeding 43°C include *Corynebacterium thermoaminogenes*, such as *Corynebacterium thermoaminogenes* FERM 9244, FERM 9245, FERM 9246 and FERM 9247.

[0150] A strain having a further improved productivity of the target product can be obtained using the thus reconstructed strain as the parent strain and further breeding it using the conventional mutagenesis method, the gene amplification method, the gene replacement method using the recombinant DNA technique, the transduction method or the cell fusion method. Accordingly, the microorganism of the present invention includes, but is not limited to, a mutant, a cell fusion strain, a transformant, a transductant or a recombinant strain constructed by using recombinant DNA techniques, so long as it is a producing strain obtained via the step of accumulating at least two effective mutations in a coryneform bacteria in the course of breeding.

[0151] When a mutation point judged as being harmful to the growth or production is specified, on the other hand, it is examined whether or not the producing strain used at present contains the mutation point. When it has the mutation, it can be returned to the wild type gene and thus a further useful production strain can be bred.

[0152] The breeding method as described above is applicable to microorganisms, other than coryneform bacteria, which have industrially advantageous properties (for example, microorganisms capable of quickly utilizing less exp n-sive carbon sources, microorganisms capable of growing at higher temperatures).

- 7. Production and utilization of polynucleotide array
- (1) Production of polynucleotide array

10

15

25

30

35

40

50

55

[0153] A polynucleotide array can be produced using the polynucleotide or oligonucleotide of the present invention obtained in the above items 1 and 2.

[0154] Examples include a p lynucleotide array comprising a s lid support to which at least one of a polynucle tid comprising the nucleotide sequence represented by SEQ ID NOS:2 to 3501, a polynucleotide which hybridizes with the polynucleotide under stringent conditions, and a polynucleotide comprising 10 to 200 continuous nucleotides in the nucleotide sequence of the polynucleotide is adher d; and a polynucleotide array comprising a solid support to

which at least one of a polynucleotide encoding a polypeptide comprising the amino acid sequence represent d by any one of SEQ ID NOS:3502 to 7001, a polynucleotide which hybridizes with the polynucleotide under stringent conditions, and a polynucleotide comprising 10 to 200 continuous bases in the nucleotide sequences of the polynucleotides is adhered.

- [0155] Polynucleotide arrays of the present invention include substrates known in the art, such as a DNA chip, a DNA microarray and a DNA macroarray, and the like, and comprises a solid support and plural polynucleotides or fragments thereof which are adhered to the surface of the solid support.
  - [0156] Examples of the solid support include a glass plate, a nylon membrane, and the like.
- [0157] The polynucleotides or fragments thereof adhered to the surface of the solid support can be adhered to the surface of the solid support using the general technique for preparing arrays. Namely, a method in which they are adhered to a chemically surface-treated solid support, for example, to which a polycation such as polylysine or the lik has been adhered (*Nat. Genet.*, 21: 15-19 (1999)). The chemically surface-treated supports are commercially available and the commercially available solid product can be used as the solid support of the polynucleotide array according to the present invention.
- [0158] As the polynucleotides or oligonucleotides adhered to the solid support, the polynucleotides and oligonucleotides of the present invention obtained in the above items 1 and 2 can be used.
  - [0159] The analysis described below can be efficiently performed by adhering the polynucleotides or oligonucleotides to the solid support at a high density, though a high fixation density is not always necessary.
- [0160] Apparatus for achieving a high fixation density, such as an arrayer robot or the like, is commercially available from Takara Shuzo (GMS417 Arrayer), and the commercially available product can be used.
  - [0161] Also, the oligonucleotides of the present invention can be synthesized directly on the solid support by the photolithography method or the like (*Nat. Genet., 21*: 20-24 (1999)). In this method, a linker having a protective group which can be removed by light irradiation is first adhered to a solid support, such as a slide glass or the like. Then, it is irradiated with light through a mask (a photolithograph mask) permeating light exclusively at a definite part of the adhesion part. Next, an oligonucleotide having a protective group which can be removed by light irradiation is added to the part. Thus, a ligation reaction with the nucleotide arises exclusively at the irradiated part. By repeating this procedure, oligonucleotides, each having a desired sequence, different from each other can be synthesized in respective parts. Usually, the oligonucleotides to be synthesized have a length of 10 to 30 nucleotides.
- 30 (2) Use of polynucleotide array

25

40

- [0162] The following procedures (a) and (b) can be carried out using the polynucleotide array prepared in the abov (1).
- (a) Identification of mutation point of coryneform bacterium mutant and analysis of expression amount and expression profile of gene encoded by genome
  - [0163] By subjecting a gene derived from a mutant of coryneform bacteria or an examined gene to the following steps (i) to (iv), the mutation point of the gene can be identified or the expression amount and expression profile of the gene can be analyzed:
    - (i) producing a polynucleotide array by the method of the above (1);
    - (ii) incubating polynucleotides immobilized on the polynucleotide array together with the labeled gene derived from a mutant of the coryneform bacterium using the polynucleotide array produced in the above (i) under hybridization conditions;
    - (iii) detecting the hybridization; and
    - (iv) analyzing the hybridization data.
- [0164] The gene derived from a mutant of coryneform bacteria or the examined gene include a gene relating to biosynthesis of at least one selected from amino acids, nucleic acids, vitamins, saccharides, organic acids, and analogues thereof.
  - [0165] The method will be described in detail.
  - [0166] A single nucleotide polymorphism (SNP) in a human region of 2,300 kb has been identified using polynucleotide arrays (*Science, 280*: 1077-82 (1998)). In accordance with the method of identifying SNP and methods described in *Science, 278*: 680-686 (1997); *Proc. Natl. Acad. Sci. USA, 96*: 12833-38 (1999); *Science, 284*: 1520-23 (1999), and the like using the polynucleotide array produced in the above (1) and a nucleic acid molecule (DNA, RNA) derived from coryneform bacteria in the method of the hybridization, a mutation point of a useful mutant, which is useful in producing an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, or the like can b identified and the gen

expression amount and the expression profile ther of can be analyzed.

[0167] The nucleic acid molecule (DNA, RNA) derived from the coryneform bacteria can be obtained according to the general method described in *Molecular Cloning*, 2nd ed. or the like. mRNA derived from *Corynebacterium glutamicum* can also be obtained by the method of Bormann et al. (*Molecular Microbiology*, 6: 317-326 (1992)) or the like.

[0168] Although ribosomal RNA (rRNA) is usually obtained in large excess in addition to the target mRNA, the analysis is not seriously disturbed thereby.

[0169] The resulting nucleic acid molecule derived from coryneform bacteria is labeled. Labeling can be carried out according to a method using a fluorescent dye, a method using a radioisotope or the like.

[0170] Specific examples include a labeling method in which psoralen-biotin is crosslinked with RNA extracted from a microorganism and, after hybridization reaction, a fluorescent dye having streptoavidin bound thereto is bound to the biotin moiety (*Nat. Biotechnol., 16*: 45-48 (1998)); a labeling method in which a reverse transcription reaction is carried out using RNA extracted from a microorganism as a template and random primers as primers, and dUTP having a fluorescent dye (for example, Cy3, Cy5) (manufactured by Amersham Pharmacia Biotech) is incorporated into cDNA (*Proc. Natl. Acad. Sci. USA, 96*: 12833-38 (1999)); and the like.

[0171] The labeling specificity can be improved by replacing the random primers by sequences complementary to the 3'-end of ORF (*J. Bacteriol., 181*: 6425-40 (1999)).

[0172] In the hybridization method, the hybridization and subsequent washing can be carried out by the general method (*Nat. Bioctechnol.*, 14: 1675-80 (1996), or the like).

[0173] Subsequently, the hybridization intensity is measured depending on the hybridization amount of the nucleic acid molecule used in the labeling. Thus, the mutation point can be identified and the expression amount of the gene can be calculated.

[0174] The hybridization intensity can be measured by visualizing the fluorescent signal, radioactivity, luminescence dose, and the like, using a laser confocal microscope, a CCD camera, a radiation imaging device (for example, STORM manufactured by Amersham Pharmacia Biotech), and the like, and then quantifying the thus visualized data.

25 [0175] A polynucleotide array on a solid support can also be analyzed and quantified using a commercially availabl apparatus, such as GMS418 Array Scanner (manufactured by Takara Shuzo) or the like.

[0176] The gene expression amount can be analyzed using a commercially available software (for example, ImaGene manufactured by Takara Shuzo; Array Gauge manufactured by Fuji Photo Film; ImageQuant manufactured by Amersham Pharmacia Biotech, or the like).

30 [0177] A fluctuation in the expression amount of a specific gene can be monitored using a nucleic acid molecule obtained in the time course of culture as the nucleic acid molecule derived from coryneform bacteria. The cultur conditions can be optimized by analyzing the fluctuation.

[0178] The expression profile of the microorganism at the total gene level (namely, which genes among a great number of genes encoded by the genome have been expressed and the expression ratio thereof) can be determined using a nucleic acid molecule having the sequences of many genes determined from the full genome sequence of the microorganism. Thus, the expression amount of the genes determined by the full genome sequence can be analyzed and, in its turn, the biological conditions of the microorganism can be recognized as the expression pattern at the full gene level.

40 (b) Confirmation of the presence of gene homologous to examined gene in coryneform bacteria

[0179] Whether or not a gene homologous to the examined gene, which is present in an organism other than coryneform bacteria, is present in coryneform bacteria can be detected using the polynucleotide array prepared in the above (1).

[0180] This detection can be carried out by a method in which an examined gene which is present in an organism other than coryneform bacteria is used instead of the nucleic acid molecule derived from coryneform bacteria used in the above identification/analysis method of (1).

8. Recording medium storing full genome nucleotide sequence and ORF data and being readable by a computer and methods for using the same

[0181] The term "recording medium or storage device which is readable by a computer" means a recording medium or storage medium which can be directly readout and accessed with a computer. Examples include magnetic recording media, such as a floppy disk, a hard disk, a magnetic tape, and the like; optical recording media, such as CD-ROM, CD-R, CD-RW, DVD-ROM, DVD-RAM, DVD-RW, and the like; lectric recording media, such as RAM, ROM, and the like; and hybrids in these categories (for example, magn tic/optical recording media, such as MO and the like).

[0182] Instruments for recording or inputting in or on the recording medium r instruments or devices for reading out the information in the recording medium can be appropriately select d, depending on the type of the recording medium

20

10

15

20

35

50

and the access devic—utilized. Also, various data processing programs, software, comparator and formats are used for recording and utilizing the polynucleotide sequence information or the like, of the present invention in the recording medium. The information can be expressed in the form of a binary file, a text file or an ASCII file formatted with commercially available software, for example. Moreover, software for accessing the sequence information is available and known to one of ordinary skill in the art.

[0183] Examples of the information to be recorded in the above-described medium include the full genome nucleotide sequence information of coryneform bacteria as obtained in the above item 2, the nucleotide sequence information of ORF, the amino acid sequence information encoded by the ORF, and the functional information of polynucleotides coding for the amino acid sequences.

- [0184] The recording medium or storage device which is readable by a computer according to the present invention refers to a medium in which the information of the present invention has been recorded. Examples include recording media or storage devices which are readable by a computer storing the nucleotide sequence information represented by SEQ ID NOS:1 to 3501, the amino acid sequence information represented by SEQ ID NOS:3502 to 7001, the functional information of the nucleotide sequences represented by SEQ ID NOS:1 to 3501, the functional information of the amino acid sequences represented by SEQ ID NOS:3502 to 7001, and the information listed in Table 1 below and the like.
  - 9. System based on a computer using the recording medium of the present invention which is readable by a computer
- [0185] The term "system based on a computer" as used herein refers a system composed of hardware device(s), software device(s), and data recording device(s) which are used for analyzing the data recorded in the recording m dium of the present invention which is readable by a computer.
  - [0186] The hardware device(s) are, for example, composed of an input unit, a data recording unit, a central processing unit and an output unit collectively or individually.
- [0187] By the software device(s), the data recorded in the recording medium of the present invention are searched or analyzed using the recorded data and the hardware device(s) as described herein. Specifically, the software divice (s) contain at least one program which acts on or with the system in order to screen, analyze or compare biologically meaningful structures or information from the nucleotide sequences, amino acid sequences and the like recorded in the recording medium according to the present invention.
- [0188] Examples of the software device(s) for identifying ORF and EMF domains include GeneMark (Nuc. Acids. Res., 22: 4756-67 (1994)), GeneHacker (Protein, Nucleic Acid and Enzyme, 42: 3001-07 (1997)), Glimmer (The Institute of Genomic Research; Nuc. Acids. Res., 26: 544-548 (1998)) and the like. In the process of using such a softwar device, the default (initial setting) parameters are usually used, although the parameters can be changed, if necessary, in a manner known to one of ordinary skill in the art.
- [0189] Examples of the software device(s) for identifying a genome domain or a polypeptide domain analogous to the target sequence or the target structural motif (homology searching) include FASTA, BLAST, Smith-Waterman, GenetyxMac (manufactured by Software Development), GCG Package (manufactured by Genetic Computer Group), GenCore (manufactured by Compugen), and the like. In the process of using such a software device, the default (initial setting) parameters are usually used, although the parameters can be changed, if necessary, in a manner known to one of ordinary skill in the art.
  - [0190] Such a recording medium storing the full genome sequence data is useful in preparing a polynucleotide array by which the expression amount of a gene encoded by the genome DNA of coryneform bacteria and the expression profile at the total gene level of the microorganism, namely, which genes among many genes encoded by the genome have been expressed and the expression ratio thereof, can be determined.
- [0191] The data recording device(s) provided by the present invention are, for example, memory device(s) for recording the data recorded in the recording medium of the present invention and target sequence or target structural molif data, or the like, and a memory accessing device(s) for accessing the same.
  - [0192] Namely, the system based on a computer according to the present invention comprises the following:
  - (i) a user input device that inputs the information stored in the recording medium of the present invention, and target sequence or target structure motif information;
    - (ii) a data storage device for at least temporarily storing the input information;
    - (iii) a comparator that compares the information stored in the recording medium of the present invention with the target sequence or target structure motif information, recorded by the data storing device of (ii) for screening and analyzing nucleotide sequence information which is coincident with or analogous to the target sequence or target structure motif information; and
    - (iv) an output device that shows a screening or analyzing result obtained by the comparator.

50

[0193] This system is usable in the methods in items 2 to 5 as described above for searching and analyzing the ORF and EMF domains, target sequence, target structural motif, etc. of a coryneform bacterium, searching homologs, searching and analyzing isozymes, determining the biosynthesis pathway and the signal transmission pathway, and identifying spots which have been found in the proteome analysis. The term "homologs" as us different includes both of orthologs and paralogs.

10. Production of polypeptide using ORF derived from coryneform bacteria

10

15

20

25

30

35

40

- [0194] The polypeptide of the present invention can be produced using a polynucleotide comprising the ORF obtained in the above item 2. Specifically, the polypeptide of the present invention can be produced by expressing the polynucleotide of the present invention or a fragment thereof in a host cell, using the method described in *Molecular Cloning*, 2nd ed., *Current Protocols in Molecular Biology*, and the like, for example, according to the following method.
  - [0195] A DNA fragment having a suitable length containing a part encoding the polypeptide is prepared from the full length ORF sequence, if necessary.
- [0196] Also, DNA in which nucleotides in a nucleotide sequence at a part encoding the polypeptide of the present invention are replaced to give a codon suitable for expression of the host cell, if necessary. The DNA is useful for efficiently producing the polypeptide of the present invention.
  - [0197] A recombinant vector is prepared by inserting the DNA fragment into the downstream of a promoter in a suitable expression vector.
- [0198] The recombinant vector is introduced to a host cell suitable for the expression vector.
- [0199] Any of bacteria, yeasts, animal cells, insect cells, plant cells, and the like can be used as the host cell so long as it can be expressed in the gene of interest.
- **[0200]** Examples of the expression vector include those which can replicate autonomously in the above-described host cell or can be integrated into chromosome and have a promoter at such a position that the DNA encoding the polypeptide of the present invention can be transcribed.
- [0201] When a procaryote cell, such as a bacterium or the like, is used as the host cell, it is preferred that the recombinant vector containing the DNA encoding the polypeptide of the present invention can replicate autonomously in the bacterium and is a recombinant vector constituted by, at least a promoter, a ribosome binding sequence, the DNA of the present invention and a transcription termination sequence. A promoter controlling gene can also be contained therewith in operable combination.
- [0202] Examples of the expression vectors include a vector plasmid which is replicable in Corynebacterium glutamicum, such as pCGI (Japanese Published Unexamined Patent Application No. 134500/82), pCG2 (Japanese Publish d Unexamined Patent Application No. 35197/83), pCG4 (Japanese Published Unexamined Patent Application No. 183799/82), pCG11 (Japanese Published Unexamined Patent Application No. 134500/82), pCG116, pCE54 and pCB101 (Japanese Published Unexamined Patent Application No. 105999/83), pCE51, pCE52 and pCE53 (Mol. Gen. Genet., 196: 175-178 (1984)), and the like; a vector plasmid which is replicable in Escherichia coli, such as pET3 and pET11 (manufactured by Stratagene), pBAD, pThioHis and pTrcHis (manufactured by Invitrogen), pKK223-3 and pGEX2T (manufactured by Amersham Pharmacia Biotech), and the like; and pBTrp2, pBTac1 and pBTac2 (manufactured by Boehringer Mannheim Co.), pSE280 (manufactured by Invitrogen), pGEMEX-1 (manufactured by Prom ga), pQE-8 (manufactured by QIAGEN), pKYP10 (Japanese Published Unexamined Patent Application No. 110600/83), pKYP200 (Agric. Biol. Chem., 48: 669 (1984)), pLSA1 (Agric. Biol. Chem., 53: 277 (1989)), pGEL1 (Proc. Natl. Acad. Sci. USA, 82: 4306 (1985)), pBluescript II SK(-) (manufactured by Stratagene), pTrs30 (prepared from Escherichia coli JM109/pTrS30 (FERM BP-5407)), pTrs32 (prepared from Escherichia coli JM109/pTrS32 (FERM BP-5408)), pGHA2 (prepared from Escherichia coli IGHA2 (FERM B-400), Japanese Published Unexamined Patent Application No. 221091/85), pGKA2 (prepared from Escherichia coli IGKA2 (FERM BP-6798), Japanese Published Unexamined Patent Application No. 221091/85), pTerm2 (U.S. Patents 4,686,191, 4,939,094 and 5,160,735), pSupex, pUB110, pTP5, pC194 and pEG400 (J. Bacteriol., 172: 2392 (1990)), pGEX (manufactured by Pharmacia), pET system (manufactured by Novagen), and the like.
- [0203] Any promoter can be used so long as it can function in the host cell. Examples include promoters derived from *Escherichia coli*, phage and the like, such as *trp* promoter ( $P_{trp}$ ), *lac* promoter,  $P_L$  promoter,  $P_R$  promot r,  $P_R$  promoter and the like. Also, artificially designed and modified promoters, such as a promoter in which two  $P_{trp}$  are linked in series ( $P_{trp}$ ×2), *tac* promoter, *lac*T7 promoter *let* promoter and the like, can be used.
- [0204] It is preferred to use a plasmid in which the space between Shine-Dalgamo sequence which is the ribosome binding sequence and the initiation c don is adjusted t an appropriate distance (for example, 6 to 18 nucleotides).
- 55 [0205] The transcription termination sequence is n\_t always necessary for the expression of the DNA of the present invention. However, it is preferred t\_arrange the transcription terminating sequence at just d\_wnstream of th\_structural gene.
  - [0206] On of ordinary skill in the art will appreciate that the codons of the above-described elements may be opti-

miz d, in a known manner, depending on the host cells and environmental conditions utilized.

[0207] Examples of the host cell include microorganisms belonging to the genus Escherichia, the genus Serratia, the genus Bacillus, the genus Brevibacterium, the genus Corynebacterium, the genus Microbacterium, the genus Pseudomonas, and the like. Specific examples include Escherichia coli XL1-Blue, Escherichia coli XL2-Blue, Escherichia coli DH1, Escherichia coli MC1000, Escherichia coli KY3276, Escherichia coli W1485, Escherichia coli JM109, Escherichia coli HB101, Escherichia coli No. 49, Escherichia coli W3110, Escherichia coli NY49, Escherichia coli Gl698, Escherichia coli TB1, Serratia ficaria, Serratia fonticola, Serratia liquefaciens, Serratia marcescens, Bacillus subtilis, Bacillus amyloliquefaciens, Corynebacterium ammonia genes, Brevibacterium immariophilum ATCC 14068, Brevibacterium saccharolyticum ATCC 14066, Corynebacterium glutamicum ATCC 13032, Corynebacterium glutamicum ATCC 13869, Corynebacterium glutamicum ATCC 14067 (prior genus and species: Brevibacterium flavum), Corynebacterium lactofermentum), Corynebacterium acetoacidophilum ATCC 13870, Corynebacterium thermoaminogenes FERM 9244. Microbacterium ammoniaphilum ATCC 15354, Pseudomonas putida, Pseudomonas sp. D-0110, and the like.

[0208] When Corynebacterium glutamicum or an analogous microorganism is used as a host, an EMF necessary for expressing the polypeptide is not always contained in the vector so long as the polynucleotide of the present invention contains an EMF. When the EMF is not contained in the polynucleotide, it is necessary to prepare the EMF separately and ligate it so as to be in operable combination. Also, when a higher expression amount or specific expression regulation is necessary, it is necessary to ligate the EMF corresponding thereto so as to put the EMF in operable combination with the polynucleotide. Examples of using an externally ligated EMF are disclosed in Microbiology, 142: 1297-1309 (1996).

[0209] With regard to the method for the introduction of the recombinant vector, any method for introducing DNA into the above-described host cells, such as a method in which a calcium ion is used (*Proc. Natl. Acad. Sci. USA, 69*: 2110 (1972)), a protoplast method (Japanese Published Unexamined Patent Application No. 2483942/88), the methods described in *Genc, 17*: 107 (1982) and *Molecular & General Genetics, 168*: 111 (1979) and the like, can be used.

[0210] When yeast is used as the host cell, examples of the expression vector include pYES2 (manufactured by Invitrogen), YEp13 (ATCC 37115), YEp24 (ATCC 37051), YCp50 (ATCC 37419), pHS19, pHS15, and the like.

[0211] Any promoter can be used so long as it can be expressed in yeast. Examples include a promoter of a gene in the glycolytic pathway, such as hexose kinase and the like, PHO5 promoter, PGK promoter, GAP promoter, ADH promoter, gal 1 promoter, gal 10 promoter, a heat shock protein promoter, MF all promoter, CUP 1 promoter, and the like.

[0212] Examples of the host cell include microorganisms belonging to the genus Saccharomyces, the genus Schizosaccharomyces, the genus Trichosporon, the genus Schwanniomyces, the genus Pichia, the genus Candida and the like. Specific examples include Saccharomyces cerevisiae, Schizosaccharomyces pombe, Kluyveromyces lactis, Trichosporon pullulans, Schwanniomyces alluvius, Candida utilis and the like.

[0213] With regard to the method for the introduction of the recombinant vector, any method for introducing DNA into yeast, such as an electroporation method (*Methods. Enzymol., 194*: 182 (1990)), a spheroplast method (*Proc. Natl. Acad. Sci. USA, 75*: 1929 (1978)), a lithium acetate method (*J. Bacteriol., 153*: 163 (1983)), a method described in *Proc. Natl. Acad. Sci. USA, 75*: 1929 (1978) and the like, can be used.

[0214] When animal cells are used as the host cells, examples of the expression vector include pcDNA3.1, pSinR p5 and pCEP4 (manufactured by Invitorogen), pRev-Tre (manufactured by Clontech), pAxCAwt (manufactured by Takara Shuzo), pcDNAI and pcDM8 (manufactured by Funakoshi), pAGE107 (Japanese Published Unexamined Patent Application No. 22979/91; Cytotechnology, 3:133 (1990)), pAS3-3 (Japanese Published Unexamined Patent Application No. 227075/90), pcDM8 (Nature, 329: 840 (1987)), pcDNAI/Amp (manufactured by Invitrogen), pREP4 (manufactured by Invitrogen), pAGE103 (J. Biochem., 101: 1307 (1987)), pAGE210, and the like.

[0215] Any promoter can be used so long as it can function in animal cells. Examples include a promoter of IE (immediate early) gene of cytomegalovirus (CMV), an early promoter of SV40, a promoter of retrovirus, a metallothionein promoter, a heat shock promoter, SR $\alpha$  promoter, and the like. Also, the enhancer of the IE gene of human CMV can be used together with the promoter.

[0216] Examples of the host cell include human Namalwa cell, monkey COS cell, Chinese hamster CHO cell, HST5637 (Japanese Published Unexamined Patent Application No. 299/88), and the like.

[0217] The method for introduction of the recombinant vector into animal cells is not particularly limited, so long as it is the general method for introducing DNA into animal cells, such as an electroporation method (*Cytotechnology, 3*: 133 (1990)), a calcium phosphate method (Japanese Published Unexamined Patent Application No. 227075/90), a lipofection method (*Proc. Natl. Acad. Sci. USA, 84*, 7413 (1987)), the method described in *Virology, 52*: 456 (1973), and the like.

[0218] When insect cells are used as the host cells, the polypeptide can be xpressed, for example, by the method described in *Bacurovirus Expression Vectors, A Laboratory Manual*, W.H. Freeman and Company, N w York (1992), *Bio/Technology*, 6: 47 (1988), r the like.

[0219] Specifically, a recombinant gene transfer vector and bacurovirus are simultaneously inserted into insect cells

5

10

15

20

25

30

35

40

to obtain a recombinant virus in an insect cell culture sup matant, and then the insect cells ar infected with the resulting recombinant virus to express the polypeptide.

[0220] Examples of the gene introducing vector used in the method include pBlueBac4.5, pVL1392, pVL1393 and pBlueBacIII (manufactured by Invitrogen), and the like.

[0221] Examples of the bacurovirus include Autographa californica nuclear polyhedrosis virus with which insects of the family *Barathra* are infected, and the like.

[0222] Examples of the insect cells include *Spodoptera frugiperda* oocytes Sf9 and Sf21 (*Bacurovirus Expression Vectors, A Laboratory Manual, W.H.* Freeman and Company, New York (1992)), *Trichoplusia ni* oocyte High 5 (manufactured by Invitrogen) and the like.

[0223] The method for simultaneously incorporating the above-described recombinant gene transfer vector and the above-described bacurovirus for the preparation of the recombinant virus include calcium phosphate method (Japan se Published Unexamined Patent Application No. 227075/90), lipofection method (*Proc. Natl. Acad. Sci. USA, 84*: 7413 (1987)) and the like.

10

15

20

25

30

35

40

50

55

[0224] When plant cells are used as the host cells, examples of expression vector include a Ti plasmid, a tobacco mosaic virus vector, and the like.

[0225] Any promoter can be used so long as it can be expressed in plant cells. Examples include 35S promoter of cauliflower mosaic virus (CaMV), rice actin 1 promoter, and the like.

[0226] Examples of the host cells include plant cells and the like, such as tobacco, potato, tomato, carrot, soybean, rape, alfalfa, rice, wheat, barley, and the like.

[0227] The method for introducing the recombinant vector is not particularly limited, so long as it is the general method for introducing DNA into plant cells, such as the *Agrobacterium* method (Japanese Published Unexamined Pat nt Application No. 140885/84, Japanese Published Unexamined Patent Application No. 70080/85, WO 94/00977), the electroporation method (Japanese Published Unexamined Patent Application No. 251887/85), the particle gun method (Japanese Patents 2606856 and 2517813), and the like.

[0228] The transformant of the present invention includes a transformant containing the polypeptide of the present invention *per se* rather than as a recombinant vector, that is, a transformant containing the polypeptide of the present invention which is integrated into a chromosome of the host, in addition to the transformant containing the above recombinant vector.

[0229] When expressed in yeasts, animal cells, insect cells or plant cells, a glycopolypeptide or glycosylated polypeptide can be obtained.

[0230] The polypeptide can be produced by culturing the thus obtained transformant of the present invention in a culture medium to produce and accumulate the polypeptide of the present invention or any polypeptide expressed under the control of an EMF of the present invention, and recovering the polypeptide from the culture.

[0231] Culturing of the transformant of the present invention in a culture medium is carried out according to the conventional method as used in culturing of the host.

[0232] When the transformant of the present invention is obtained using a prokaryote, such as *Escherichia coli* or the like, or a eukaryote, such as yeast or the like, as the host, the transformant is cultured.

[0233] Any of a natural medium and a synthetic medium can be used, so long as it contains a carbon source, a nitrogen source, an inorganic salt and the like which can be assimilated by the transformant and can perform culturing of the transformant efficiently.

[0234] Examples of the carbon source include those which can be assimilated by the transformant, such as carbohydrates (for example, glucose, fructose, sucrose, molasses containing them, starch, starch hydrolysate, and the like), organic acids (for example, acetic acid, propionic acid, and the like), and alcohols (for example, ethanol, propanol, and the like).

[0235] Examples of the nitrogen source include ammonia, various ammonium salts of inorganic acids or organic acids (for example, ammonium chloride, ammonium sulfate, ammonium acetate, ammonium phosphate, and the like), other nitrogen-containing compounds, peptone, meat extract, yeast extract, corn steep liquor, casein hydrolysate, soybean meat and soybean meat hydrolysate, various fermented cells and hydrolysates thereof, and the like.

[0236] Examples of inorganic salt include potassium dihydrogen phosphate, dipotassium hydrogen phosphate, magnesium phosphate, magnesium sulfate, sodium chloride, ferrous sulfate, manganese sulfate, copper sulfate, calcium carbonate, and the like.

[0237] The culturing is carried out under acrobic conditions by shaking culture, submerged-acration stirring culture or the like. The culturing temperature is preferably from 15 to 40°C, and the culturing time is generally from 16 hours to 7 days. The pH of the medium is pr ferably maintained at 3.0 to 9.0 during the culturing. The pH can be adjust d using an inorganic or organic acid, an alkali solution, urea, calcium carbonate, ammonia, or the lik

[0238] Also, antibiotics, such as ampicillin, tetracycline, and the like, can be added to the medium during the culturing, if necessary.

[0239] When a microorganism transformed with a recombinant vector containing an inducible promoter is cultured,

an inducer can be added to the medium, if necessary.

5

10

20

25

35

45

[0240] For example, isopropyl-β-D-thiogalactopyranoside (IPTG) or the like can be added to the medium when a microorganism transformed with a recombinant vector containing *lac* promoter is cultured, or indoleacrylic acid (IAA) or the like can by added thereto when a microorganism transformed with an expression vector containing *trp* promoter is cultured.

[0241] Examples of the medium used in culturing a transformant obtained using animal cells as the host cells include RPMI 1640 medium (*The Journal of the American Medical Association, 199.* 519 (1967)), Eagle's MEM medium (*Science, 122*: 501 (1952)), Dulbecco's modified MEM medium (*Virology, 8,* 396 (1959)), 199 Medium (*Proceeding of the Society for the Biological Medicine, 73*:1 (1950)), the above-described media to which fetal calf serum has been added, and the like.

[0242] The culturing is carried out generally at a pH of 6 to 8 and a temperature of 30 to 40°C in the presence of 5% CO<sub>2</sub> for 1 to 7 days.

[0243] Also, if necessary, antibiotics, such as kanamycin, penicillin, and the like, can be added to the medium during the culturing.

15 [0244] Examples of the medium used in culturing a transformant obtained using insect cells as the host cells include TNM-FH medium (manufactured by Pharmingen), Sf-900 II SFM (manufactured by Life Technologies), ExCell 400 and ExCell 405 (manufactured by JRH Biosciences), Grace's Insect Medium (Nature, 195: 788 (1962)), and the like.

[0245] The culturing is carried out generally at a pH of 6 to 7 and a temperature of 25 to 30°C for 1 to 5 days.

[0246] Additionally, antibiotics, such as gentamicin and the like, can be added to the medium during the culturing, if necessary.

[0247] A transformant obtained by using a plant cell as the host cell can be used as the cell or after differentiating to a plant cell or organ. Examples of the medium used in the culturing of the transformant include Murashige and Sk og (MS) medium, White medium, media to which a plant hormone, such as auxin, cytokinine, or the like has been added, and the like.

[0248] The culturing is carried out generally at a pH of 5 to 9 and a temperature of 20 to 40°C for 3 to 60 days.

[0249] Also, antibiotics, such as kanamycin, hygromycin and the like, can be added to the medium during the culturing, if necessary.

[0250] As described above, the polypeptide can be produced by culturing a transformant derived from a micro r-ganism, animal cell or plant cell containing a recombinant vector to which a DNA encoding the polypeptide of the present invention has been inserted according to the general culturing method to produce and accumulate the polypeptide, and recovering the polypeptide from the culture.

[0251] The process of gene expression may include secretion of the encoded protein production or fusion protein expression and the like in accordance with the methods described in *Molecular Cloning*, 2nd ed., in addition to direct expression

[0252] The method for producing the polypeptide of the present invention includes a method of intracellular expr ssion in a host cell, a method of extracellular secretion from a host cell, or a method of production on a host cell membrane outer envelope. The method can be selected by changing the host cell employed or the structure of the polypeptid produced.

[0253] When the polypeptide of the present invention is produced in a host cell or on a host cell membrane outer envelope, the polypeptide can be positively secreted extracellularly according to, for example, the method of Paulson et al. (J. Biol. Chem., 264: 17619 (1989)), the method of Lowe et al. (Proc. Natl. Acad. Sci. USA, 86: 8227 (1989); Genes Develop., 4: 1288 (1990)), and/or the methods described in Japanese Published Unexamined Patent Application No. 336963/93, WO 94/23021, and the like.

[0254] Specifically, the polypeptide of the present invention can be positively secreted extracellularly by expressing it in the form that a signal peptide has been added to the foreground of a polypeptide containing an active site of the polypeptide of the present invention according to the recombinant DNA technique.

[0255] Furthermore, the amount produced can be increased using a gene amplification system, such as by use of a dihydrofolate reductase gene or the like according to the method described in Japanese Published Unexamined Patent Application No. 227075/90.

50 [0256] Moreover, the polypeptide of the present invention can be produced by a transgenic animal individual (transgenic plant).

[0257] When the transformant is the animal individual or plant individual, the polypeptide of the present invention can be produced by breeding or cultivating it so as to produce and accumulate the polypeptide, and recovering the polypeptide from the animal individual or plant individual.

[0258] Examples f the method for producing the polypeptide of the present invention using the animal individual include a method for producing the polypeptide of the present invention in an animal developed by insinting a gine according to methods known to those of ordinary skill in the art (American Journal of Clinical Nutrition, 63: 639S (1996), American Journal of Clinical Nutrition, 63: 627S (1996), Bio/Technology, 9: 830 (1991)).

[0259] In the animal individual, the polypeptide can be produced by breeding a transgenic nonhuman animal to which the DNA encoding the polypeptide of the present invention has been inserted to produce and accumulate the polypeptide in the animal, and recovering the polypeptide from the animal. Examples of the production and accumulation place in the animal include milk (Japanese Published Unexamined Patent Application No. 309192/88), egg and the like of the animal. Any promoter can be used, so long as it can be expressed in the animal. Suitable examples include an  $\alpha$ -casein promoter, a ( $\beta$ -casein promoter, a  $\beta$ -lactoglobulin promoter, a whey acidic protein promoter, and the like, which are specific for mammary glandular cells.

[0260] Examples of the method for producing the polypeptide of the present invention using the plant individual include a method for producing the polypeptide of the present invention by cultivating a transgenic plant to which the DNA encoding the protein of the present invention by a known method (*Tissue Culture, 20* (1994), *Tissue Culture, 21* (1994), *Trends in Biotechnology, 15:* 45 (1997)) to produce and accumulate the polypeptide in the plant, and recovering the polypeptide from the plant.

[0261] The polypeptide according to the present invention can also be obtained by translation in vitro.

10

15

20

25

30

35

40

45

[0262] The polypeptide of the present invention can be produced by a translation system *in vitro*. There are, for example, two *in vitro* translation methods which may be used, namely, a method using RNA as a template and another method using DNA as a template. The template RNA includes the whole RNA, mRNA, an *in vitro* transcription product, and the like. The template DNA includes a plasmid containing a transcriptional promoter and a target gene integrated therein and downstream of the initiation site, a PCR/RT-PCR product and the like. To select the most suitable system for the *in vitro* translation, the origin of the gene encoding the protein to be synthesized (prokaryotic cell/eucaryotic cell), the type of the template (DNA/RNA), the purpose of using the synthesized protein and the like should be considered. *In vitro* translation kits having various characteristics are commercially available from many companies (Boehringer Mannheim, Promega, Stratagene, or the like), and every kit can be used in producing the polypeptide according to the present invention.

[0263] Transcription/translation of a DNA nucleotide sequence cloned into a plasmid containing a T7 promoter can be carried out using an *in vitro* transcription/translation system *E. coli* T7 S30 Extract System for Circular DNA (manufactured by Promega, catalogue No. L1130). Also, transcription/translation using, as a template, a linear prokaryotic DNA of a supercoil non-sensitive promoter, such as *lac*UV5, *tac*, λPL(con), λPL, or the like, can be carried out using an *in vitro* transcription/translation system *E. coli* S30 Extract System for Linear Templates (manufactured by Promega, catalogue No. L1030). Examples of the linear prokaryotic DNA used as a template include a DNA fragment, a PCR-amplified DNA product, a duplicated oligonucleotide ligation, an *in vitro* transcriptional RNA, a prokaryotic RNA, and the like

[0264] In addition to the production of the polypeptide according to the present invention, synthesis of a radioactiv labeled protein, confirmation of the expression capability of a cloned gene, analysis of the function of transcriptional reaction or translation reaction, and the like can be carried out using this system.

[0265] The polypeptide produced by the transformant of the present invention can be isolated and purified using the general method for isolating and purifying an enzyme. For example, when the polypeptide of the present invention is expressed as a soluble product in the host cells, the cells are collected by centrifugation after cultivation, suspended in an aqueous buffer, and disrupted using an ultrasonicator, a French press, a Manton Gaulin homogenizer, a Dynomill, or the like to obtain a cell-free extract. From the supernatant obtained by centrifuging the cell-free extract, a purified product can be obtained by the general method used for isolating and purifying an enzyme, for example, solvent extraction, salting out using ammonium sulfate or the like, desalting, precipitation using an organic solvent, anion exchange chromatography using a resin, such as S-Sepharose, DIAION HPA-75 (manufactured by Mitsubishi Chemical) or the like, cation exchange chromatography using a resin, such as S-Sepharose FF (manufactured by Pharmacia) or the like, hydrophobic chromatography using a resin, such as butyl sepharose, phenyl sepharose or the like, gel filtration using a molecular sieve, affinity chromatography, chromatofocusing, or electrophoresis, such as isoelectronic focusing or the like, alone or in combination thereof.

[0266] When the polypeptide is expressed as an insoluble product in the host cells, the cells are collected in the same manner, disrupted and centrifuged to recover the insoluble product of the polypeptide as the precipitate fraction. Next, the insoluble product of the polypeptide is solubilized with a protein denaturing agent. The solubilized solution is diluted or dialyzed to lower the concentration of the protein denaturing agent in the solution. Thus, the normal configuration of the polypeptide is reconstituted. After the procedure, a purified product of the polypeptide can be obtained by a purification/isolation method similar to the above.

[0267] When the polypeptide of the present invention or its derivative (for example, a polypeptide formed by adding a sugar chain thereto) is secreted out of cells, the pilip ptide or its dirivative can be collect dirithe culture supernatant. Namily, the culture supernatant is obtained by treating the culture medium in a treatment similar to the above (for example, cintrifugation). Thin, a purified product can be obtained from the culture medium using a purification/isolation method similar to the above.

[0268] The polypeptide obtained by the above method is within the scope of the polypeptide of the pres int invintion,

and examples include a polypeptide encoded by a polynucleotide comprising the nucleotide sequence selected from SEQ ID NOS:2 to 3431, and a polypeptide comprising an amino acid sequence represented by any one of SEQ ID NOS:3502 to 6931.

[0269] Furthermore, a polypeptide comprising an amino acid sequence in which at least one amino acids is deleted, replaced, inserted or added in the amino acid sequence of the polypeptide and having substantially the same activity as that of the polypeptide is included in the scope of the present invention. The term "substantially the same activity as that of the polypeptide" means the same activity represented by the inherent function, enzyme activity or the like possessed by the polypeptide which has not been deleted, replaced, inserted or added. The polypeptide can be obtained using a method for introducing part-specific mutation(s) described in, for example, *Molecular Cloning*, 2nd ed., *Current Protocols in Molecular Biology, Nuc. Acids. Res.*, 10: 6487 (1982), *Proc. Natl. Acad. Sci. USA*, 79: 6409 (1982), *Gene, 34*: 315 (1985), *Nuc. Acids. Res.*, 13: 4431 (1985), *Proc. Natl. Acad. Sci. USA*, 82: 488 (1985) and the like. For example, the polypeptide can be obtained by introducing mutation(s) to DNA encoding a polypeptide having the amino acid sequence represented by any one of SEQ ID NOS:3502 to 6931. The number of the amino acids which are deleted, replaced, inserted or added is not particularly limited; however, it is usually 1 to the order of tens, preferably 1 to 20, more preferably 1 to 10, and most preferably 1 to 5, amino acids.

[0270] The at least one amino acid deletion, replacement, insertion or addition in the amino acid sequence of the polypeptide of the present invention is used herein to refer to that at least one amino acid is deleted, replaced, inserted or added to at one or plural positions in the amino acid sequence. The deletion, replacement, insertion or addition may be caused in the same amino acid sequence simultaneously. Also, the amino acid residue replaced, inserted or added can be natural or non-natural. Examples of the natural amino acid residue include L-alanine, L-asparagine, L-asparatic acid, L-glutamine, L-glutamic acid, glycine, L-histidine, L-isoleucine, L-leucine, L-lysine, L-methionine, L-phenylalanine, L-proline, L-serine, L-threonine, L-tryptophan, L-tyrosine, L-valine, L-cysteine, and the like.

[0271] Herein, examples of amino acid residues which are replaced with each other are shown below. The amino acid residues in the same group can be replaced with each other.

Group A:

10

15

20

25

30

[0272] leucine, isoleucine, norleucine, valine, norvaline, alanine, 2-aminobutanoic acid, methionine, O-methylserine, t-butylglycine, t-butylglycine, cyclohexylalanine;

Group B:

[0273] asparatic acid, glutamic acid, isoasparatic acid, isoglutamic acid, 2-aminoadipic acid, 2-aminosuberic acid;

35 Group C:

[0274] asparagine, glutamine;

Group D:

[0275] lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid;

Group E:

45 [0276] proline, 3-hydroxyproline, 4-hydroxyproline;

Group F:

[0277] serine, threonine, homoserine:

Group G:

50

55

[0278] phenylalanine, tyrosine.

[0279] Also, in order that the resulting mutant polypeptide has substantially the same activity as that of the polypeptid which has not been mutated, it is preferred that the mutant polypeptid has a homology of 60% or more, preferably 80% or more, and particularly preferably 95% or more, with the pelypeptide which has not been mutated, when calculated, for example, using default (initial setting) parameters by a homology searching software, such as BLAST, FASTA, or the like.

[0280] Also, the polypeptid of the present invention can be produced by a chemical synthesis method, such as Fmoc (fluorenylmethyloxycarbonyl) method, tBoc (t-butyloxycarbonyl) method, or the like. It can also be synthesized using a peptide synthesizer manufactured by Advanced ChemTech, Perkin-Elmer, Pharmacia, Protein Technology Instrument, Synthecell-Vega, PerSeptive, Shimadzu Corporation, or the like.

[0281] The transformant of the present invention can be used for objects other than the production of the polypeptide of the present invention.

[0282] Specifically, at least one component selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof can be produced by culturing the transformant containing the polynucleotide or recombinant vector of the present invention in a medium to produce and accumulate at least one component selected from amino acids, nucleic acids, vitamins, saccharides, organic acids, and analogues thereof, and recovering the same from the medium.

[0283] The biosynthesis pathways, decomposition pathways and regulatory mechanisms of physiologically active substances such as amino acids, nucleic acids, vitamins, saccharides, organic acids and analogues thereof differ from organism to organism. The productivity of such a physiologically active substance can be improved using these differences, specifically by introducing a heterogeneous gene relating to the biosynthesis thereof. For example, the content of lysine, which is one of the essential amino acids, in a plant seed was improved by introducing a synthase gene derived from a bacterium (WO 93/19190). Also, arginine is excessively produced in a culture by introducing an arginine synthase gene derived from *Escherichia coli* (Japanese Examined Patent Publication 23750/93).

[0284] To produce such a physiologically active substance, the transformant according to the present invention can be cultured by the same method as employed in culturing the transformant for producing the polypeptide of the present invention as described above. Also, the physiologically active substance can be recovered from the culture medium in combination with, for example, the ion exchange resin method, the precipitation method and other known methods. [0285] Examples of methods known to one of ordinary skill in the art include electroporation, calcium transfection, the protoplast method, the method using a phage, and the like, when the host is a bacterium; and microinjection, calcium phosphate transfection, the positively charged lipid-mediated method and the method using a virus, and the like, when the host is a eukaryote (*Molecular Cloning*, 2nd ed.; Spector et al., Cells/a laboratory manual, Cold Spring Harbour Laboratory Press, 1998)). Examples of the host include prokaryotes, lower eukaryotes (for example, yeasts), higher eukaryotes (for example, mammals), and cells isolated therefrom. As the state of a recombinant polynucleotide fragment present in the host cells, it can be integrated into the chromosome of the host. Alternatively, it can be integrated into a factor (for example, a plasmid) having an independent replication unit outside the chromosome. These transformants are usable in producing the polypeptides of the present invention encoded by the ORF of the genome of Corynebacterium glutamicum, the polynucleotides of the present invention and fragments thereof. Alternatively, they can be used in producing arbitrary polypeptides under the regulation by an EMF of the present invention.

#### 11. Preparation of antibody recognizing the polypeptide of the present invention

[0286] An antibody which recognizes the polypeptide of the present invention, such as a polyclonal antibody, a monoclonal antibody, or the like, can be produced using, as an antigen, a purified product of the polypeptide of the present invention or a partial fragment polypeptide of the polypeptide or a peptide having a partial amino acid sequence of the polypeptide of the present invention.

### (1) Production of polyclonal antibody

[0287] A polyclonal antibody can be produced using, as an antigen, a purified product of the polypeptide of the present invention, a partial fragment polypeptide of the polypeptide, or a peptide having a partial amino acid sequence of the polypeptide of the present invention, and immunizing an animal with the same.

[0288] Examples of the animal to be immunized include rabbits, goals, rats, mice, hamsters, chickens and the like.

[0289] A dosage of the antigen is preferably 50 to 100 µg per animal.

[0290] When the peptide is used as the antigen, it is preferably a peptide covalently bonded to a carrier protein, such as keyhole limpet haemocyanin, bovine thyroglobulin, or the like. The peptide used as the antigen can be synthesized by a peptide synthesizer.

[0291] The administration of the antigen is, for example, carried out 3 to 10 times at the intervals of 1 or 2 weeks after the first administration. On the 3rd to 7th day after each administration, a blood sample is collected from the venous plexus of the eyeground, and it is confirmed that the serum reacts with the antigen by the enzyme immunoassay (Enzyme-linked Immunosorbent Assay (ELISA), Igaku Shoin (1976); Antibodies - A Laboratory Manual, Cold Spring Harbor Laboratory (1988)) or the like.

[0292] Serum is obtained from the immunized non-human mammal with a sufficient antibody titer against the antigen used for the immunization, and the serum is isolated and purified to obtain a polyclonal antibody.

5

10

15

20

25

30

35

40

[0293] Examples of the method for the isolation and purification include centrifugation, salting out by 40-50% saturated ammonium sulfate, caprylic acid precipitation (*Antibodies, A Laboratory manual,* Cold Spring Harbor Laboratory (1988)), or chromatography using a DEAE-Sepharose column, an anion exchange column, a protein A- or G-column, a gel filtration column, and the like, alone or in combination thereof, by methods known to those of ordinary skill in the art.

(2) Production of monoclonal antibody

5

15

25

35

- (a) Preparation of antibody-producing cell
- 10 [0294] A rat having a serum showing an enough antibody titer against a partial fragment polypeptide of the polypeptide of the present invention used for immunization is used as a supply source of an antibody-producing cell.
  - [0295] On the 3rd to 7th day after the antigen substance is finally administered the rat showing the antibody titer, the spleen is excised.
  - [0296] The spleen is cut to pieces in MEM medium (manufactured by Nissui Pharmaceutical), loosened using a pair of forceps, followed by centrifugation at 1,200 rpm for 5 minutes, and the resulting supernatant is discarded.
  - [0297] The spleen in the precipitated fraction is treated with a Tris-ammonium chloride buffer (pH 7.65) for 1 to 2 minutes to eliminate erythrocytes and washed three times with MEM medium, and the resulting spleen cells are used as antibody-producing cells.
- (b) Preparation of myeloma cells

[0298] As myeloma cells, an established cell line obtained from mouse or rat is used. Examples of useful cell lin s include those derived from a mouse, such as P3-X63Ag8-U1 (hereinafter referred to as "P3-U1") (*Curr. Topics in Microbiol. Immunol., 81*: 1 (1978); *Europ. J. Immunol., 6*: 511 (1976)); SP2/O-Agl4 (SP-2) (*Nature, 276*: 269 (1978)): P3-X63-Ag8653 (653) (*J. Immunol., 123*: 1548 (1979)); P3-X63-Ag8 (X63) cell line (*Nature, 256*: 495 (1975)), and th like, which are 8-azaguanine-resistant mouse (BALB/c) myeloma cell lines. These cell lines are subcultured in 8-azaguanine medium (medium in which, to a medium obtained by adding 1.5 mmol/l glutamine, 5×10-5 mol/l 2-mercaptoethanol, 10 μg/ml gentamicin and 10% fetal calf serum (FCS) (manufactured by CSL) to RPMI-1640 medium (hereinafter referred to as the "normal medium"), 8-azaguanine is further added at 15 μg/ml) and cultured in the normal medium 3 or 4 days before cell fusion, and 2×10<sup>7</sup> or more of the cells are used for the fusion.

(c) Production of hybridoma

[0299] The antibody-producing cells obtained in (a) and the myeloma cells obtained in (b) are washed with MEM medium or PBS (disodium hydrogen phosphate: 1.83 g, sodium dihydrogen phosphate: 0.21 g, sodium chloride: 7.65 g, distilled water: 1 liter, pH: 7.2) and mixed to give a ratio of antibody-producing cells: myeloma cells = 5: 1 to 10: 1, followed by centrifugation at 1,200 rpm for 5 minutes, and the supernatant is discarded.

[0300] The cells in the resulting precipitated fraction were thoroughly loosened, 0.2 to 1 ml of a mixed solution of 2 g of polyethylene glycol-1000 (PEG-1000), 2 ml of MEM medium and 0.7 ml of dimethylsulfoxide (DMSO) per 10<sup>8</sup> antibody-producing cells is added to the cells under stirring at 37°C, and then 1 to 2 ml of MEM medium is further added thereto several times at 1 to 2 minute intervals.

[0301] After the addition, MEM medium is added to give a total amount of 50 ml. The resulting prepared solution is centrifuged at 900 rpm for 5 minutes, and then the supernatant is discarded. The cells in the resulting precipitated fraction were gently loosened and then gently suspended in 100 ml of HAT medium (the normal medium to which  $10^{-4}$  mol/l hypoxanthine,  $1.5 \times 10^{-5}$  mol/l thymidine and  $4 \times 10^{-7}$  mol/l aminopterin have been added) by repeated drawing up into and discharging from a measuring pipette.

[0302] The suspension is poured into a 96 well culture plate at 100  $\mu$ l/well and cultured at 37°C for 7 to 14 days in a 5% CO<sub>2</sub> incubator.

[0303] After culturing, a part of the culture supernatant is recovered, and a hybridoma which specifically reacts with a partial fragment polypeptide of the polypeptide of the present invention is selected according to the enzyme immunoassay described in *Antibodies, A Laboratory manual,* Cold Spring Harbor Laboratory, Chapter 14 (1998) and the like. [0304] A specific example of the enzyme immunoassay is described below.

[0305] The partial fragment polypeptide of the polypeptide of the present invention used as the antigen in the immunization is spread on a suitable plate, is allowed to react with a hybrid ma culturing supernatant or a purified antibody obtained in (d) described below as a first antibility, and is further allowed to react with an anti-ration anti-mouse immunoglobulin antibody labeled with an enzyme, a chemical luminous substance, a radioactive substance or the like as a second antibody for reaction suitable for the labeled substance. A hybridoma which specifically reacts with the polypeptide of the present invintion is selected as a hybridoma capable of producing a monoclonal antibody of the present

invention.

5

20

25

35

40

[0306] Cloning is repeated using the hybridoma twice by limiting dilution analysis (HT medium (a medium in which aminopterin has been removed from HAT medium) is firstly used, and the normal medium is secondly used), and a hybridoma which is stable and contains a sufficient amount of antibody titer is selected as a hybridoma capable of producing a monoclonal antibody of the present invention.

### (d) Preparation of monoclonal antibody

[0307] The monoclonal antibody-producing hybridoma cells obtained in (c) are injected intraperitoneally into 8- to 10-week-old mice or nude mice treated with pristane (intraperitoneal administration of 0.5 ml of 2,6,10,14-tetrameth-ylpentadecane (pristane), followed by 2 weeks of feeding) at  $5\times10^6$  to  $20\times10^6$  cells/animal. The hybridoma causes ascites tumor in 10 to 21 days.

[0308] The ascitic fluid is collected from the mice or nude mice, and centrifuged to remove solid contents at 3000 rpm for 5 minutes.

15 [0309] A monoclonal antibody can be purified and isolated from the resulting supernatant according to the method similar to that used in the polyclonal antibody.

[0310] The subclass of the antibody can be determined using a mouse monoclonal antibody typing kit or a rat monoclonal antibody typing kit. The polypeptide amount can be determined by the Lowry method or by calculation based on the absorbance at 280 nm.

[0311] The antibody obtained in the above is within the scope of the antibody of the present invention.

[0312] The antibody can be used for the general assay using an antibody, such as a radioactive material labeled immunoassay (RIA), competitive binding assay, an immunotissue chemical staining method (ABC method, CSA method, etc.), immunoprecipitation, Western blotting, ELISA assay, and the like (*An introduction to Radioimmunoassay and Related Techniques*, Elsevier Science (1986); *Techniques in Immunocytochemistry*, Academic Press, Vol. 1 (1982),

Vol. 2 (1983) & Vol. 3 (1985); Practice and Theory of Enzyme Immunoassays, Elsevier Science (1985); Enzyme-linked Immunosorbent Assay (ELISA), Igaku Shoin (1976); Antibodies - A Laboratory Manual, Cold Spring Harbor laboratory (1988); Monoclonal Antibody Experiment Manual, Kodansha Scientific (1987); Second Series Biochemical Experiment Course, Vol. 5, Immunobiochemistry Research Method, Tokyo Kagaku Dojin (1986)).

[0313] The antibody of the present invention can be used as it is or after being labeled with a label.

[0314] Examples of the label include radioisotope, an affinity label (e.g., biotin, avidin, or the like), an enzyme label (e.g., horseradish peroxidase, alkaline phosphatase, or the like), a fluorescence label (e.g., FITC, rhodamine, or the like), a label using a rhodamine atom, (*J. Histochem. Cytochem.*, 18: 315 (1970); Meth. Enzym., 62: 308 (1979); Immunol., 109: 129 (1972); J. Immunol., Meth., 13: 215 (1979)), and the like.

[0315] Expression of the polypeptide of the present invention, fluctuation of the expression, the presence or absence of structural change of the polypeptide, and the presence or absence in an organism other than coryneform bacteria of a polypeptide corresponding to the polypeptide can be analyzed using the antibody or the labeled antibody by the above assay, or a polypeptide array or proteome analysis described below.

[0316] Furthermore, the polypeptide recognized by the antibody can be purified by immunoaffinity chromatography using the antibody of the present invention.

#### 12. Production and use of polypeptide array

### (1) Production of polypeptide array

[0317] A polypeptide array can be produced using the polypeptide of the present invention obtained in the above item 10 or the antibody of the present invention obtained in the above Item 11.

[0318] The polypeptide array of the present invention includes protein chips, and comprises a solid support and the polypeptide or antibody of the present invention adhered to the surface of the solid support.

[0319] Examples of the solid support include plastic such as polycarbonate or the like; an acrylic resin, such as polyacrylamide or the like; complex carbohydrates, such as agarose, sepharose, or the like; silica; a silica-based material, carbon, a metal, inorganic glass, latex beads, and the like.

[0320] The polypeptides or antibodies according to the present invention can be adhered to the surface of the solid support according to the method described in *Biotechniques*, 27: 1258-61 (1999); *Molecular Medicine Today*, 5: 326-7 (1999); *Handbook of Experimental Immunology*, 4th edition, Blackwell Scientific Publications, Chapter 10 (1986); *Meth.* 

Enzym., 34 (1974); Advances in Experimental Medicine and Biology, 42 (1974); U.S. Patent 4,681,870; U.S. Patent 4,282,287; U.S. Patent 4,762,881, or the like.

[0321] The analysis described herein can be efficiently performed by adhering the polypeptide or antibody of the present invention to the solid support at a high density, though a high fixation density is not always necessary.

#### (2) Use of polypeptide array

10

15

20

25

30

35

40

45

50

[0322] A polypeptide or a compound capable of binding to and interacting with the polypeptides of the present invention adhered to the array can be identified using the polypeptide array to which the polypeptides of the present invention have been adhered thereto as described in the above (1).

[0323] Specifically, a polypeptide or a compound capable of binding to and interacting with the polypeptides of the present invention can be identified by subjecting the polypeptides of the present invention to the following steps (i) to (iv):

- (i) preparing a polypeptide array having the polypeptide of the present invention adhered thereto by the method of the above (1);
- (ii) incubating the polypeptide immobilized on the polypeptide array together with at least one of a second polypeptide or compound;
- (iii) detecting any complex formed between the at least one of a second polypeptide or compound and the polypeptide immobilized on the array using, for example, a label bound to the at least one of a second polypeptide or compound, or a secondary label which specifically binds to the complex or to a component of the complex after unbound material has been removed; and
- (iv) analyzing the detection data.

[0324] Specific examples of the polypeptide array to which the polypeptide of the present invention has been adhered include a polypeptide array containing a solid support to which at least one of a polypeptide containing an amino acid sequence selected from SEQ ID NOS:3502 to 7001, a polypeptide containing an amino acid sequence in which at least one amino acids is deleted, replaced, inserted or added in the amino acid sequence of the polypeptide and having substantially the same activity as that of the polypeptide, a polypeptide containing an amino acid sequence having a homology of 60% or more with the amino acid sequences of the polypeptide and having substantially the same activity as that of the polypeptides, a partial fragment polypeptide, and a peptide comprising an amino acid sequence of a part of a polypeptide.

[0325] The amount of production of a polypeptide derived from coryneform bacteria can be analyzed using a polypeptide array to which the antibody of the present invention has been adhered in the above (1).

[0326] Specifically, the expression amount of a gene derived from a mutant of coryneform bacteria can be analyzed by subjecting the gene to the following steps (i) to (iv):

- (i) preparing a polypeptide array by the method of the above (1);
- (ii) incubating the polypeptide array (the first antibody) together with a polypeptide derived from a mutant of coryneform bacteria;
- (iii) detecting the polypeptide bound to the polypeptide immobilized on the array using a labeled second antibody of the present invention; and
- (iv) analyzing the detection data.

[0327] Specific examples of the polypeptide array to which the antibody of the present invention is adhered include a polypeptide array comprising a solid support to which at least one of an antibody which recognizes a polypeptide comprising an amino acid sequence selected from SEQ ID NOS:3502 to 7001, a polypeptide comprising an amino acid sequence in which at least one amino acids is deleted, replaced, inserted or added in the amino acid sequence of the polypeptide and having substantially the same activity as that of the polypeptide, a polypeptide comprising an amino acid sequence having a homology of 60% or more with the amino acid sequences of the polypeptide and having substantially the same activity as that of the polypeptides, a partial fragment polypeptide, or a peptide comprising an amino acid sequence of a part of a polypeptide.

[0328] A fluctuation in an expression amount of a specific polypeptide can be monitored using a polypeptide obtained in the time course of culture as the polypeptide derived from coryneform bacteria. The culturing conditions can be optimized by analyzing the fluctuation.

- [0329] When a polypeptide derived from a mutant of coryneform bacteria is used, a mutated polypeptide can be detected.
  - 13. Identification of useful mutation in mutant by proteome analysis
- [0330] Usually, the proteome is used herein to refer to a method wherein a polypeptide is separated by tw dimensional electrophoresis and the separated polypeptide is digested with an enzyme, followed by identification of the polypeptid using a mass spectrometer (MS) and searching a data base.
  - [0331] The two dimensional electrophoresis means an electrophoretic method which is performed by combining two

lectrophoretic procedures having different principles. For xample, polypeptides are separated depending on molecular weight in the primary electrophoresis. Next, the gel is rotated by 90° or 180° and the secondary electrophoresis is carried out depending on isoelectric point. Thus, various separation patterns can be achieved (JIS K 3600 2474).

[0332] In searching the data base, the amino acid sequence information of the polypeptides of the present invention

and the recording medium of the present invention provide for in the above items 2 and 8 can be used.

[0333] The proteome analysis of a coryneform bacterium and its mutant makes it possible to identify a polypeptide showing a fluctuation therebetween.

[0334] The proteome analysis of a wild type strain of coryneform bacteria and a production strain showing an improved productivity of a target product makes it possible to efficiently identify a mutation protein which is useful in breeding for improving the productivity of a target product or a protein of which expression amount is fluctuated.

[0335] Specifically, a wild type strain of coryneform bacteria and a lysine-producing strain thereof are each subjected to the proteome analysis. Then, a spot increased in the lysine-producing strain, compared with the wild type strain, is found and a data base is searched so that a polypeptide showing an increase in yield in accordance with an increase in the lysine productivity can be identified. For example, as a result of the proteome analysis on a wild type strain and a lysine-producing strain, the productivity of the catalase having the amino acid sequence represented by SEQ ID NO:

3785 is increased in the lysine-producing mutant.

[0336] As a result that a protein having a high expression level is identified by proteome analysis using the nucleotide sequence information and the amino acid sequence information, of the genome of the coryneform bacteria of the present invention, and a recording medium storing the sequences, the nucleotide sequence of the gene encoding this protein and the nucleotide sequence in the upstream thereof can be searched at the same time, and thus, a nucleotide sequence having a high expression promoter can be efficiently selected.

[0337] In the proteome analysis, a spot on the two-dimentional electrophoresis gel showing a fluctuation is sometimes derived from a modified protein. However, the modified protein can be efficiently identified using the recording medium storing the nucleotide sequence information, the amino acid sequence information, of the genome of coryneform bacteria, and the recording medium storing the sequences, according to the present invention.

[0338] Moreover, a useful mutation point in a useful mutant can be easily specified by searching a nucleotide squence (nucleotide sequence of promoters, ORF, or the like) relating to the thus identified protein using a recording medium storing the nucleotide sequence information and the amino acid sequence information, of the genome of coryneform bacteria of the present invention, and a recording medium storing the sequences and using a primer designed on the basis of the detected nucleotide sequence. As a result that the useful mutation point is specified, an industrially useful mutant having the useful mutation or other useful mutation derived therefrom can be easily bred.

[0339] The present invention will be explained in detail below based on Examples. However, the present invention

is not limited thereto.

## 35 Example 1

15

25

30

40

45

55

Determination of the full nucleotide sequence of genome of Corynebacterium glutamicum

[0340] The full nucleotide sequence of the genome of *Corynebacterium glutamicum* was determined based on the whole genome shotgun method (*Science*, *269*: 496-512 (1995)). In this method, a genome library was prepared and the terminal sequences were determined at random. Subsequently, these sequences were ligated on a comput r to cover the full genome. Specifically, the following procedure was carried out.

(1) Preparation of genome DNA of Corynebacterium glutamicum ATCC 13032

[0341] Corynebacterium glutamicum ATCC 13032 was cultured in BY medium (7 g/l meat extract, 10 g/l pepton , 3 g/l sodium chloride, 5 g/l yeast extract, pH 7.2) containing 1% of glycine at 30°C overnight and the cells were collected by centrifugation. After washing with STE buffer (10.3% sucrose, 25 mmol/l Tris hydrochloride, 25 mmol/l EDTA, pH 8.0), the cells were suspended in 10 ml of STE buffer containing 10 mg/ml lysozyme, followed by gently shaking at 37°C for 1 hour. Then, 2 ml of 10% SDS was added thereto to lyse the cells, and the resultant mixture was maintained at 65°C for 10 minutes and then cooled to room temperature. Then, 10 ml of Tris-neutralized phenol was added thereto, followed by gently shaking at room temperature for 30 minutes and centrifugation (15,000 × g, 20 minutes, 20°C). The aqueous layer was separated and subjected to extraction with phenol/chloroform and extraction with chloroform (twice) in the same manner. To the aqueous layer, 3 mol/l sodium acetate solution (pH 5.2) and is propanol were added at 1/10 times volume and twice volume, respectively, followed by gently stirring to precipitate the genome DNA. The genome DNA was dissolved again in 3 ml of TE buffer (10 mmol/l Tris hydrochloride, 1 mmol/l EDTA, pH 8.0) containing 0.02 mg/ml of RNase and maintained at 37°C for 45 minutes. The extractions with phenol, phenol/chl roform and chloroform were carried out successively in the same manner as the above. The genome DNA was subjected to iso-

propanol precipitation. The thus formed genome DNA precipitate was washed with 70% ethanol three times, followed by air-drying, and dissolved in 1.25 ml of TE buffer to give a genome DNA solution (concentration: 0.1 mg/ml).

(2) Construction of a shotgun library

5

10

15

20

30

35

40

50

55

[0342] TE buffer was added to 0.01 mg of the thus prepared genome DNA of *Corynebacterium glutamicum* ATCC 13032 to give a total volume of 0.4 ml, and the mixture was treated with a sonicator (Yamato Powersonic Model 150) at an output of 20 continuously for 5 seconds to obtain fragments of 1 to 10 kb. The genome fragments were bluntended using a DNA blunting kit (manufactured by Takara Shuzo) and then fractionated by 6% polyacrylamide gel electrophoresis. Genome fragments of 1 to 2 kb were cut out from the gel, and 0.3 ml MG elution buffer (0.5 mol/l ammonium acetate, 10 mmol/l magnesium acetate, 1 mmol/l EDTA, 0.1% SDS) was added thereto, followed by shaking at 37°C overnight to elute DNA. The DNA eluate was treated with phenol/chloroform, and then precipitated with ethanol to obtain a genome library insert. The total insert and 500 ng of pUC18 *Smal*/BAP (manufactured by Amersham Pharmacia Biotech) were ligated at 16°C for 40 hours.

[0343] The ligation product was precipitated with ethanol and dissolved in 0.01 ml of TE buffer. The ligation solution (0.001 ml) was introduced into 0.04 ml of *E. coli* ELECTRO MAX DH10B (manufactured by Life Technologies) by the electroporation under conditions according to the manufacture's instructions. The mixture was spread on LB plate medium (LB medium (10 g/l bactotrypton, 5 g/l yeast extract, 10 g/l sodium chloride, pH 7.0) containing 1.6% of agar) containing 0.1 mg/ml ampicillin, 0.1 mg/ml X-gal and 1 mmol/l isopropyl-β-D-thiogalactopyranoside (IPTG) and cultured at 37°C overnight.

[0344] The transformant obtained from colonies formed on the plate medium was stationarily cultured in a 96-w II titer plate having 0.05 ml of LB medium containing 0.1 mg/ml ampicillin at 37°C overnight. Then, 0.05 ml of LB medium containing 20% glycerol was added thereto, followed by stirring to obtain a glycerol stock.

25 (3) Construction of cosmid library

[0345] About 0.1 mg of the genome DNA of Corynebacterium glutamicum ATCC 13032 was partially digested with Sau3Al (manufactured by Takara Shuzo) and then ultracentrifuged (26,000 rpm, 18 hours, 20°C) under 10 to 40% sucrose density gradient obtained using 10% and 40% sucrose buffers (1 mol/l NaCl, 20 mmol/l Tris hydrochloride, 5 mmol/l EDTA, 10% or 40% sucrose, pH 8.0). After the centrifugation, the solution thus separated was fractionated into tubes at 1 ml in each tube. After confirming the DNA fragment length of each fraction by agarose gel electrophoresis, a fraction containing a large amount of DNA fragment of about 40 kb was precipitated with ethanol.

[0346] The DNA fragment was ligated to the BamHI site of superCos1 (manufactured by Stratagene) in accordance with the manufacture's instructions. The ligation product was incorporated into Escherichia coli XL-1-BlueMR strain (manufactured by Stratagene) using Gigapack III Gold Packaging Extract (manufactured by Stratagene) in accordance with the manufacture's instructions. The Escherichia coli was spread on LB plate medium containing 0.1 mg/ml ampicillin and cultured therein at 37°C overnight to isolate colonies. The resulting colonies were stationarily cultured at 37°C overnight in a 96-well titer plate containing 0.05 ml of the LB medium containing 0.1 mg/ml ampicillin in each well. LB medium containing 20% glycerol (0.05 ml) was added thereto, followed by stirring to obtain a glycerol stock.

(4) Determination of nucleotide sequence

(4-1) Preparation of template

[0347] The full nucleotide sequence of Corynebacterium glutamicum ATCC 13032 was determined mainly based on the whole genome shotgun method. The template used in the whole genome shotgun method was prepared by the PCR method using the library prepared in the above (2).

[0348] Specifically, the clone derived from the whole genome shotgun library was inoculated using a replicator (manufactured by GENETIX) into each well of a 96-well plate containing the LB medium containing 0.1 mg/ml of ampicillin at 0.08 ml per each well and then stationarily cultured at 37°C overnight.

[0349] Next, the culturing solution was transported using a copy plate (manufactured by Tokken) into a 96-well reaction plate (manufactured by PE Biosystems) containing a PCR reaction solution (TaKaRa Ex Taq (manufactured by Takara Shuzo)) at 0.08 ml per each well. Then, PCR was carried out in accordance with the protocol by Makino et al. (DNA Research, 5: 1-9 (1998)) using GeneAmp PCR System 9700 (manufactured by PE Biosystems) to amplify the inserted fragment.

[0350] The excessive primers and nucleotides were eliminated using a kit for purifying a PCR production (manufactured by Amersham Pharmacia Biotech) and the residue was used as the template in the sequencing reaction.

[0351] Some nucleotide sequences were determined using a double-stranded DNA plasmid as a template.

[0352] The double-stranded DNA plasmid as the timplate was obtain id by the following method.

[0353] The clone derived from the whole genome shotgun library was inoculated into a 24- or 96-well plate containing a  $2 \times YT$  medium (16 g/l bactotrypton, 10 g/l yeast extract, 5 g/l sodium chloride, pH 7.0) containing 0.05 mg/ml ampicillin at 1.5 ml per each well and then cultured under shaking at 37°C overnight.

[0354] The double-stranded DNA plasmid was prepared from the culturing solution using an automatic plasmid preparing machine, KURABO PI-50 (manufactured by Kurabo Industries) or a multiscreen (manufactured by Millipore) in accordance with the protocol provided by the manufacturer.

[0355] To purify the double-stranded DNA plasmid using the multiscreen, Biomek 2000 (manufactured by Beckman Coulter) or the like was employed.

[0356] The thus obtained double-stranded DNA plasmid was dissolved in water to give a concentration of about 0.1 mg/ml and used as the template in sequencing.

### (4-2) Sequencing reaction

10

15

20

25

50

55

[0357] To 6 μl of a solution of ABI PRISM BigDye Terminator Cycle Sequencing Ready Reaction Kit (manufactured by PE Biosystems), an M13 regular direction primer (M13-21) or an M13 reverse direction primer (M13REV) (*DNA Research*, *5*: 1-9 (1998) and the template prepared in the above (4-1) (the PCR product or the plasmid) were added to give 10 μl of a sequencing reaction solution. The primers and the templates were used in an amount of 1.6 pmol and an amount of 50 to 200 ng, respectively.

[0358] Dye terminator sequencing reaction of 45 cycles was carried out with GeneAmp PCR System 9700 (manufactured by PE Biosystems) using the reaction solution. The cycle parameter was determined in accordance with the manufacturer's instruction accompanying ABI PRISM BigDye Terminator Cycle Sequencing Ready Reaction Kit. Th sample was purified using MultiScreen HV plate (manufactured by Millipore) according to the manufacture's instructions. The thus purified reaction product was precipitated with ethanol, followed by drying, and then stored in the dark at -30°C.

[0359] The dry reaction product was analyzed by ABI PRISM 377 DNA Sequencer and ABI PRISM 3700 DNA Analyzer (both manufactured by PE Biosystems) each in accordance with the manufacture's instructions.

[0360] The data of about 50,000 sequences in total (i.e., about 42,000 sequences obtained using 377 DNA Sequencer and about 8,000 reactions obtained by 3700 DNA Analyser) were transferred to a server (Alpha Server 4100: manufactured by COMPAQ) and stored. The data of these about 50,000 sequences corresponded to 6 times as much as the genome size.

#### (5) Assembly

[0361] All operations were carried out on the basis of UNIX platform. The analytical data were output in Macintosh platform using X Window System. The base call was carried out using phred (The University of Washington). The vector sequence data was deleted using SPS Cross\_Match (manufactured by Southwest Parallel Software). The assembly was carried out using SPS phrap (manufactured by Southwest Parallel Software; a high-speed version of phrap (The University of Washington)). The contig obtained by the assembly was analyzed using a graphical editor, cons d (The University of Washington). A series of the operations from the base call to the assembly were carried out simultaneously using a script phredPhrap attached to consed.

### (6) Determination of nucleotide sequence in gap part

[0362] Each cosmid in the cosmid library constructed in the above (3) was prepared by a method similar to the preparation of the double-stranded DNA plasmid described in the above (4-1). The nucleotide sequence at the end of the inserted fragment of the cosmid was determined by using ABI PRISM BigDye Terminator Cycle Sequencing Ready Reaction Kit (manufactured by PE Biosystems) according to the manufacture's instructions.

[0363] About 800 cosmid clones were sequenced at both ends to search a nucleotide sequence in the contig derived from the shotgun sequencing obtained in the above (5) coincident with the sequence. Thus, the linkage between respective cosmid clones and respective contigs were determined and mutual alignment was carried out. Furthermor, the results were compared with the physical map of *Corynebacterium glutamicum* ATCC 13032 (*Mol. Gen. Genet., 252*: 255-265 (1996) to carrying out mapping between the cosmids and the contigs.

[0364] The sign quence in the region which was not covered with thic contigs was determined by the following method.

[0365] Clones containing sequences position did at the ends of contigs were silected. Among thes clones, about 1,000 clones wherein only one end of the inserted fragment had been determined were selected and the sequence at the opposite end of the inserted fragment was determined. A shotgun library clone in a cosmid clone containing the sequences at the respective ends of the inserted fragment in two contigs was identified, the full nucleotide sequence

of the inserted fragment of this clone was det mined, and thus the nucleotide sequence of the gap part was determined. When no shotgun library clone or cosmid clone covering the gap part was available, primers complementary to the end sequences at the two contigs were prepared and the DNA fragment in the gap part was amplified by PCR. Then, sequencing was performed by the primer walking method using the amplified DNA fragment as a template or by the shotgun method in which the sequence of a shotgun clone prepared from the amplified DNA fragment was determined. Thus, the nucleotide sequence of the domain was determined.

[0366] In a region showing a low sequence precision, primers were synthesized using AUTOFINISH function and NAVIGATING function of consed (The University of Washington) and the sequence was determined by the primer walking method to improve the sequence precision. The thus determined full nucleotide sequence of the genome of Corynebacterium glutamicum ATCC 13032 strain is shown in SEQ ID NO:1.

(7) Identification of ORF and presumption of its function

[0367] ORFs in the nucleotide sequence represented by SEQ ID NO:1 were identified according to the following method. First, the ORF regions were determined using software for identifying ORF, i.e., Glimmer, GeneMark and GeneMark.hmm on UNIX platform according to the respective manual attached to the software.

[0368] Based on the data thus obtained, ORFs in the nucleotide sequence represented by SEQ ID NO:1 were identified.

[0369] The pulative function of an ORF was determined by searching the homology of the identified amino acid sequence of the ORF against an amino acid database consisting of protein-encoding domains derived from Swiss-Prot, PIR or Genpept database constituted by protein encoding domains derived from GenBank database. Frame Search (manufactured by Compugen), or by searching the homology of the identified amino acid sequence of the ORF against an amino acid database consisting of protein-encoding domains derived from Swiss-Prot, PIR or Genpept database constituted by protein encoding domains derived from GenBank database, BLAST. The nucleotide sequences of the thus determined ORFs are shown in SEQ ID NOS:2 to 3501, and the amino acid sequences encoded by these ORFs are shown in SEQ ID NOS:3502 to 7001.

[0370] In some cases of the sequence listings in the present invention, nucleotide sequences, such as TTG, TGT, GGT, and the like, other than ATG, are read as an initiating codon encoding Met.

[0371] Also, the preferred nucleotide sequences are SEQ ID NOS:2 to 355 and 357 to 3501, and the preferred amino acid sequences are shown in SEQ ID NOS:3502 to 3855 and 3857 to 7001

[0372] Table 1 shows the registration numbers in the above-described databases of sequences which were judged as having the highest homology with the nucleotide sequences of the ORFs as the results of the homology search in the amino acid sequences using the homology-searching software Frame Search (manufactured by Compugen), names of the genes of these sequences, the functions of the genes, and the matched length, identities and analogies compared with publicly known amino acid translation sequences. Moreover, the corresponding positions were confirmed via the alignment of the nucleotide sequence of an arbitrary ORF with the nucleotide sequence of SEQ ID NO:

1. Also, the positions of nucleotide sequences other than the ORFs (for example, ribosomal RNA genes, transfer RNA genes, IS sequences, and the like) on the genome were determined.

[0373] Fig. 1 shows the positions of typical genes of the Corynebacterium glutamicum ATCC 13032 on the genome.

35

10

20

25

30

35

40

45

50

cytochrome c biogenesis protein

265

57.4 64.5 70.1

29.1 31.6

Rhodobacter capsulatus ccdA

870 gp:AF'56103\_2 762 pr. A49232

17860 18736

18729 17251

19497

21

420

17670

3519 3520 3521

5 5

Coxletta burnetii corr1

hypothetical protein

155 117

repressor

36.8

Mycobacterium tuberculosis H37Rv Rv1846c

pir:F7C664

369

20073

19705

3522

22

5		Function	replication initiation protein DnaA	i.	DNA polymerase III beta chain	DNA replication protein (recF protein)	hypothetical protein	DNA tcpoisomerase (ATP- hydrolyzing)					NAGC/XYLR repressor			DNA gyrase subunit A	hypothetical membrane protein	hypothetical protein	bacterial regulatory protein, LysR type
15		Watched 'ength (a.a.)	524		390	392	174	704					422			854	112	329	268
20		Similarity (%)	9.66		81.8	79.9	58.1	88.9					50.7	-		88.1	9.69	63.5	62.3
		identity (%)	866		50.5	53.3	35.1	71.9					29.4			70.4	29.5	33.7	27.6
25		<b>9</b> 2	dnaA		atis dnaN	atis recF	ryreG	llosis					losis			losis	losis	His	noluteolus
30	Table 1	Homologous gene	Brev:bacterium flavum dnaA		Mycobacterium smegmatis dnaN	Nycobacterium smegmatis recF	Streptomyces coelicolor yreG	Mycobacterium tuberculosis H37Rv gyrB					Mycobacterium tuberculosis H37Rv			Mycobacterium tuberculosis H37Rv Rv0006 gyrA	Mycobacterium tuberculosis H37Rv Rv0007	Escherichia coli K12 yeiH	Hydrogenophilus thermoluteolus TH-1 cbbR
40		db Match	gsp:R98523		sp:DP3B_MYCSM	2 SP. RECF_MYCSM	sp:YREG_STRCO						sp:YV11_MYCTU			sp:GYRA_MYCTU	pir.E70698	sp:YEIH_ECOLI	gp:AB042619_1
		ORF (bp)	1572	324	1182	1182	534	2133	996	699	510	441	1071	261	246	2568	342	1035	894
45		Terminal (nt)	1572	1597	3473	4766	5299	7486	8795	8678	1001	9474	10107	11253	11523	14398	14746	15209	1720?
50		Initial (nt)	-	1920	2292	3585	4766	5354	7833	9466	9562	9514	11177	11523	11768	11831	14405	16243	16314
		SEQ NO (a.a)	3502	3503	3504	3505	3506	3507	3508	3509	3510	3511	3512	3513	3514	3515	3516	3517	3518
55		SEQ NO (DNA)	2	3	4	2	9	7	80	6	2	=	12	5	14	15	16	17	18

5			Function	hypothetical membrane protein	2,5-diketo-D-gluconic acic reductase	e precursor	5-nucleotidase family protein		organic hydroperoxide detoxication enzyme	ATP-dependent DNA helicase		glucan 1,4-alpha-glucosidase		ABC 3 transport family or integral membrane protein	iron(III) dicitrate transport ATP. biding protein	sugar ABC transporter, periplasmic sugar-binding protein	high affinity ribose transport protein	ribose transport ATP-bincing protein	ubunit NF-180	peptidyl-prolyl cis-trans isomerase A	hypothetical membrane protein
10				hypothetical m	2,5-diketo-D-g	5'-nucleotidase precursor	5'-nucleotidas	transposase	organic hydrop enzyme	ATP-depender		glucan 1,4-alpl	lipopretein	ABC 3 transport fa membrane protein	iron(III) dicitrate biding protein	sugar ABC transporte sugar-binding protein	high affinity ribo	ribose transpor	neurofilament subunit NF-180	peptidyl-prolyl c	hypothetical me
15			Watched ength	321	26	196	270	51	139	217		449	311	266	222	283	312	236	347	169	226
20			Similarity (%)	50.8	88.5	56.1	56.7	72.6	79.9	8.09		54.1	63.7	74.1	70.3	56.5	68.3	76.7	44.4	89.9	53.1
			Identity (%)	24.9	65.4	27.0	27.0	52.9	51.8	32.7		26.7	28.9	34.8	39.2	25.8	30.5	32.2	23.6	79.9	29.2
25	;	tinued)	jene	9	ATCC	ous netA	rans	atum ORF1	stris	ans recG		risiae	athiae	nes SF370	ecE	MSBB	bsc	A\$0		H37RV	дôb
<i>30</i>		Table 1 (continued)	Homologous gene	Mycobacterium leprae MLCB1788.18	Corynebacterium sp. ATCC 31090	Vibrio parahaemolyticus nutA	Deinococcus radiodurans DR0505	Corynebacterium striatum ORF1	Xanthomonas campestris phaseoli ohr	Thiobacillus ferrooxidans recG		Saccharomyces cerevisiae S288C YIR019C sta1	Erysipelothrix rhusiopathiae ewlA	Streptococcus pyogenes SF370 mtsC	Escherichia coli K12 fecE	Thermotoga maritima MSB8 TM0114	Escherichia coli K12 rbsC	Bacillus subtilis 168 rbsA	Petromyzon marinus	Mycobacterium leprae H37RV RV0009 ppiA	Bacillus subtilis 168 yqgP
40			db Match	gp:MLCB1788_6	pir.'40838	sp:5N <sup>-</sup> D_VIBPA	gp:AE001909_7	prf.25*3302C	prf.24*3353A	Sp. RECG_THIFE		SP:AMYH_YEAST	gp.ERU52850_1	gp:AF180520_3	sp:FECE_ECOLI		prf.1207243B	sp.RBSA_BACSU	pir 151116	sp:CYPA_MYCTU	sp YQGP_BACSU
			OR: (bp)	993	180	228	1236	165	435	1413	438	1278	954	849	657	981	1023	759	816	561	283
45			Termina (nt)	21065	21074	22124	23399	23615	24729	24885	26775	26822	28164	29117	30651	31677	32699	33457	33465	34899	35668
50			Initial (nt)	20073	21253	21597	22164	23779	24295	26297	26338	28099	29117	29965	29995	30697	3:677	32699	34280	34339	34992
			SEQ NO (a.a.)	3523	3524	3525	3526	3527	3528	3529	3530	3531	3532	3533	3534	3535	3536	3537	3538	3539	3540
<i>55</i>			SEQ NO. (DNA)	23	24	25	26	27	28	29	33	31	32	33	34		36	一十	88		6

																	$\overline{}$	$\overline{}$			
	Function	ferric enterobactin transport system permease protein		ATPase	vulnibactin utilization protein	hypothetical membrane protein	serine/threonine protein kinase	serineAhreonine protein kinase	penicillin-binding protein	stage V sporulation protein E	phosphoprotein phosphatase	hypothetical protein	hypothetical protein					phenol 2-monooxygenase	succinate-semialdehyde dehydrogenase (NAD(P)+)	hypothetical protein	hypothetical membrane protein
	Matched length (a.a.)	332		253	260	95	648	486	492	375	469	155	526					117	490	242	262
	Similarity (%)	70.5		81.8	52.7	72.6	68.7	59.1	. 66.7	65.6	70.8	66.5	38.8					63.3	78.2	57.0	64.1
	Identity (%)	40.4		51.8	26.2	40.0	40.6	31.7	33.5	31.2	44.1	38.7	23.6					29.9	46.7	27.3	29.0
Table 1 (continued)	Homologous gene	Escherichia coli K12 fepG		Vibrio cholerae viuC	Vibrio vulnificus MO6-24 viuB	Mycobacterium tube culosis H37Rv Rv0011c	Mycobacterium leprae pknB	Streptomyces caet color pksC	Streptomyces griseus pbpA	Bacillus subtilis 168 spoVE	Mycobacterium tuberculosis H37Rv ppp	Mycobacterium tuberculosis H37Rv Rv0019c	Mycobacterium tuberculosis H37Rv Rv0020c					Trichosporon cutaneum ATCC 46490	Escherichia coli K12 gabD	Bacillus subtilis yrkH	Methanococcus jannaschii MJ0441
	dɔ Match	Sp. FEPG_ECOLI		do:VC:152150 9		5	SD PKNB MYCLE	$\vdash$		sp.SP5E_BACSU	pir:H70699	plr.A70700	pir:B70700					sp.PH2M_TRICU	sp:GA3D_ECOU	SE YRKH BACSU	sp:Y441_METJA
	ORF (bp)	978	986	$\neg$		+	1938	_	1422	<del></del>	1353	462	864	147	720	219	471	954	1470	1467	789
	Terminal (nt)	38198	36247	38078	39799	40189	40576	42513	43926	45347	46669	48024	48505	49455	49897	50754	50966	54008	51626	55546	55629
	Initial (nt)	37221	17747	28202	38978	40458	475.3	43919	45347	46489	48021	48485	49368	49601	50616	50972	51436	1	53095	54080	
	SEO NO.	3541	75.42	25.43	3544	3545	35.46	3547	3548	3549	3550	3551	3552	3553	3554	3555	3556	3557	3558	1550	3560
	SEQ		42	十			A A	i	Ť	1		51	52	53	54	55	56	57	58	60	3 8

					1	-	-	_	_	<del> </del>	_				_	<del></del>		<del>,                                     </del>				
5		lion .								alt transport		tein	Insport	n-induced				lex secondary	em sensor		ator	hydroxyacid
10		Function	hypothetical protein	hypothetical protein	hypothetical protein		hypothetical protein			magnesium and cobalt transport protein		chloride channel protein	required for NMN transport	phosphate starvation-induced protein-like protein				Mg(2+ //citrate complex secondary transporter	two-component system sensor histidine kinase		transcriptional regulator	D-isomer specific 2-hydroxyacid dehydrogenase
15		Matched length (a.a.)	74	179	62		310			390		84		340				497	563		229 t	293
20		Similarity (%)	74.3	70.4	83.9		50.7			59.5		64.8	53.1	0.09				68.8	9.09		63.3	73.7
		Identity (%)	40.5	36.3	53 2		26.8			29.5		30.0	24.1	29.1				42.3	27.2		33.2	43.3
25	tinued)	ene		C6803	culosis		68.11			ulosis		M4 clcb	m pouc	ulosis					919		R.	micum
<i>30</i>	Table 1 (continued)	Homologous gene	Bacillus subtilis yrkF	Synechocystis sp. PCC6803 slr1261	Mycobacterium tuberculosis H37Rv Rv1766		Leishmania major L4768.11			Mycobacterium tuberculosis H37Rv Rv1239c corA		Zymomonas mobilis ZM4 clcb	Salmonella typhimurium phuC	Mycobacterium tuberculosis H37Rv RV2368C				Bacillus subtilis citM	Escherichia coli K12 dpiB		Escherichia coli K12 criR	Corynebacterium glutamicum unkdh
		_	i		≥r					ΣÏ												
40		db Match	SP.YRKF_BACSU	sp:YCE1_SYNY3	pir:G7C988		9P:LMFL4768_11			pir:F70952		gp:AF179611_12	SP:PNUC_SALTY	sp:PHOL_MYCTU				sp:CITM_BACSU	sp:DPIB_ECOLI		Sp.DPIA_ECOLI	gp:A=134895_1
45		ORF (bp)	291	591	174	855	840	711	1553	1113	447	1269	069	1122	132	384	765	1467	1653	570	654	912
		Terminal (nt)	55386	55680	57651	58941	59930	60662	62321	62390	63594	65458	65508	67972	68304	68251	65824	68720	72158	71474	72814	72817
50		Initial (nt)	92995	57270	57478	58087	59091	59952	69909	63506	64040	64190	66197	66851	68170	68634	09069	70186	70506	72043	72161	73728
	ا الله الله	SEO NO (a a.)	3561	3562	3563	3564	3565	3566	3567	3568	3569	3570	3571	3572	3573	3574	3575	3576	3577	3578	3579	3580
55		SEQ. NO.	19	62	63	9	- 65	99	-67	89	69	5	=	72	73	74	<del>-</del> . <del>-</del> .	76	77	78	62	ဗ္ဗ

EP 1 108 790 A2

	Function	hypothetical protein	biotin synthase	hypothetical protein	hypothetical protein		hypothetical protein	hypothetical protein	integral membrane efflux protein	creatinine deaminase			SIR2 gene family (silent information regulator)	triacylglycerol lipase	triacylglycerol lipase		transcriptional regulator	urease gammma subunit or urease structural protein	urease beta subunit	urease alpha subunit
	Matched length (a.a.)	127	334	43	85		42	84	507	394			279	251	262		171	6	162	570
	Similarity (%)	76.4	99.7	79.1	63.5		75.0	66.0	59.0	9.66			50.2	.59.0	56.1		94.7	100 0	100.0	100 0
	Identity (%)	38.6	99.4	72.1	34.1		71.0	61.0	25.6	97.2			26.2	30.7	29.4		90.6	100.0	100.0	100.0
Table 1 (continued)	Homologous gene	Streptomyces coelicolor A3(2) SCM2.03	Corynebacterium glutamicum bioB	Mycobacterium tuberculosis H37Rv Rv1590	Saccharomyces cerevisiae YKL084w		Chlamydia muridarum Nigg TC0129	Chlamydia pneumoniae	Streptomyces virginiae varS	Bacillus sp.			Saccharomyces cerevisiae hst2	Propionibacterium acnes	Propionibacterium acres		Corynebacterium glutamicum ureR	Corynebacterium glutamicum ureA	Corynebacterium glutamicum ATCC 13032 ureB	Corynebacterium glutamicum ATCC 13032 ureC
	db Match	gp:SCM2_3	sp:BIOB_CORGL	pir:H70542	sp:YK:4_YEAST		PIR F81737	GSP: Y35914	prf 25:2333A				sp:HST2_YEAST	prt 2316378A	prf 23:6378A		gp:AB029154_1	gp.AB029154_2	gp:CGL251883_2	gp CGL251883_3
	(bp)	429	1002	237	339	117	141	273	1449	1245	306	615	924	972	906	888	513	l g	486	1710
	Terminal (nt)	74272	75491	75742	76035	76469	80613	81002	82120	83691	85098	85663	87241	87561	88545	90445	90461	91473	91988	93701
	Initial (nt)	73844	74490	75506	75697	76353	80753	R1274	83568	84935	85403	86277	86318	88532	89444	89558	90973	91174	91503	91992
	SEO	3581	3582	3583	3584	3585	3586	35.B7	35.8B	3589	3590	3501	3592	3503	3594	3595	3596	3597	3598	3599
	SEO		92	83	8	85		0.7	a	8	8	3   5	92	22	8 8	35	96	97	86	66

	:																								
5			on.	otein	otein	otein	otein			protein			sp90-family)	( min 2012		e large subunit		se/P5C		Jenase	ort)	vdrolase		ne protein	
10			Function	urease accessory protein	urease accessory protein	urease accessory protein	urease accessory protein	epoxide hydrolase		valanimycin resistant protein			heat shock protein (hsp90-family)	AMP nucleosidase		acetolactate synthase large subunit		proline dehydrogenase/P5C	6 - (	aryl-alcohol dehydrogenase	pump protein (transport)	indole-3-acetyl-Asp hydrolase		hypothetical membrane protein	
15			Matched length (a.a.)	157	226	205	283	279		347			899	481		196		1297		338	513	352		106	
20			Similarity (%)	100.0	100.0	100.0	100.0	48.4		59.7			52.7	68.2		58.7		50.4		60.7	71.4	49.2		70.8	
			Identity (%)	100.0	100.0	100.0	100.0	21.2		26.5			23.8	41.0		29.6		25.8		30.2	36.5	23.0		35.9	
25		(pai		u:no	mno	Wno	E	r echA		vimF						2509		좕		rigu					
<i>30</i> <i>35</i>		Table 1 (continued)	Homologous gene	Corynebacterium glutamicum ATCC 13032 ureE	Corynebacterium glutamicum ATCC 13032 ureF	Corynebacterium glutamicum ATCC 13032 ureG	Corynebacterium glutamicum ATCC 13032 ureD	Agrobacterium radiobacter echA		Streptomyces viridifaciens vlmF			Escherichia coli K12 htpG	Escherichia coli K12 amn		Aeropyrum pernix K1 APE2509		Salmonella typhimurium putA		Phanerochaete chrysosporium aad	Escherichia coli K12 ydaH	Enterobacter agglomerans		Escherichia coli K12 yidH	
40			db Match	gp:CGL251883_4	gp:CGL251883_5	gp:CGL251883_6	gp:CGL251883_7	prf.2318326B		gp:AF148322_1			SP:HTPG_ECOLI	SP: AMN_ECOLI		pir:E72483		sp:PUTA_SALTY IS		Sp: AAD_PHACH F	sp:YDAH_ECOLI E	pri:2422424A   E		sp:YIDH_ECOLI E	
45			유) (pp)	471	678	615	849	777	699	1152	675	2775	1824	1416	579	552	99	3456	114	945	1614	1332	669	366	315
			Term nal (nt)	94199	94879	955.3	95365	98368	98189	6,676	100493	99808	101612	104909	105173	.05841	.06630	110890	111274	112318	114083	115478	114564	115943	116263
50			In tial (nt)	93726	94202	94899	95517	97144	97521	9847C	99819	101582	103435	103494	105751	106392	107289	107435	111161	111374	112470	114-47	115262	115578	115949
		<b>-</b>	SEQ NO.	3600	3601	3602	3603	3604	3605	3606	3607	3608	3509	3610	361:	3512	3513	3614	3615	3616	3617	3618	3619	3620	3621
<i>55</i>			(DNA)	5	101	102	103	104	105	106	107	108	109	110	Ξ	112	113	114	115	115	117	138	119		2

EP 1 108 790 A2

10		Function		transc:iptional repressor	methylglyoxalase	hypothetical protein	mannitol dehydrogenase	D-arabinitol transporter		galactitol utilization operon repressor	xylulose kinase		pantoatebeta-alanine ligase	3-methyl-2-oxobutanoale hydroxymethyltransferase		DNA-3-methyladenine glycosylase		esterase		carbonate dehydratase	xylose operon repressor protein	macrolide efflux protein		
15		Matched length (a a )		258	126	162	497	435		260	451		279	27.1		188		270		201	357	418		
20		Similarity (%)		59.7	78.6	64.8	70.4	68.3		64.6	68.1		100.0	100.0		97.9		69.3		53.2	49.3	61.2		
		Identity (%)		29.5	57.9	37.0	43.5	30.3		27.3	45.0		100.0	100.0		42.0		39.3		30.9	24.1	21.1		_
25	Julingen	s gene		efaciens	<b>)</b>	erculosis	rescens mtlD	niae dalT		2 gatR	Blyx susonig		lutamicum	jlutamicu:n j		a mag		ing bacterium		nermophila	23 xylR	: mef214		
30 T	(naniiiinan) i algai	Homologous gene		Agrobacterium tumefaciens accR	Bacillus subtilis yur?	Mycobacterium tuberculosis H37Rv Rv1276c	Pseudomonas fuorescens mtlD	Klebsiella pneumoniae dalT		Escherichia coli K12 gatR	Streptomyces rubiginosus xylB		Corynebacterium glutamicum ATCC 13032 panC	Corynebacterium glutamicu:n ATCC 13032 panB		Arabidopsis thallana mag		Petroleum-degrading bacterium HD-1 hde		Methanosarcina thermophila	Bacillus subtilis W23 xylR	Lactococcus lactis mef214		
<i>35</i>		db Match		sp.ACCR_AGRTU	pir.C70019	IYCTU	prf.2309180A	pr. 2321326A		sp.GATR_ECOLI	SP:XYLB_STRRU		gp:CGPAN_2	gp:CGPAN_1		Sp. 3MG_ARATH		gp:AB029896_1		SP.CAH_METTE	SP.XYLR_BACSU	gp:LLLP-<214_12		
		ORF (bp)	2052	780   5	390 lp	510 s	1509 p	1335 p	189	837 \$	1419 S	822	837	813	951	630	654	924	627	558	1143	1272	804	444
45		Terminal (nt)	116548	118810	120410	120413	120951	122507	124033	124965	126353	127992	126353	127 192	128099	.29489	130798	130815	132424	132981	132971	134207	135519	136122
50		Initial (nt)	118599	119589	120021		122459	123841	123842		1	127:71	<u></u>	3633 128004	129049	130118	130145	131738	131798	. <b>i</b> .	1	3541 135478	3642 136321	3643 136565
	٠.	SEQ NO. (a.a.)	3622	3623	3624	3625	3676	3627	3628	3629	3630	3631	3632	3633	3634	3635	3636	3637	3638		7	· <del></del>	3642	+-1
 55	eti.	SEQ NO (DNA)	122	123	124	125	126	127	128	126	130	131	132	133	134	135	136	137	138	139	140	14	142	143

					$\top$			_																		
5		Function				a	nbrane protein				1; - 9 - 1 - 1; - 4 - 6 - 6	serisitive protein	norane protein			ried on order	niane protein			e:Case		n specific for	o de la compania	mile giyeosyiase	r c	of thesis enzyme
10						cellulose synthase	hypotnetical membrane protein				chloramphonical cancilia	cinci anipinenico	Typothetical memorane protein		riotora tronsacri	hypothetical mombrose section	יואלים וופון וופון		ATD dependent to the	וווווווווווווווווווווווווווווווווווווו	nodulation protein	DNA repair system specific for	ONA-3-methyladoning aluaculas	Threanine efflux protein	hynothetical protein	doxorubicin biosynthesis enzyme
15		₹ _	(a.a.)			420	593				303	200	130		36.1	248	240		820	23	188	219	166	$\top$	T	
20		Similarity (%)				512	51.8				50.7	50 4	9		623	70.2	10.5		643		66.0	60.7	65.1	613	727	52.1
		Icentity (%)				24.3	25.1				34.7	30.3	3		32.4	34.7			33.8		40.4	34.7	39.8	34.1	50 9	31.0
25	Table 1 (continued)	s gene				efaciens celA	revisiae				qinosa rarD	2 vadS			2 abrB	2 vfcA			hroa		sarum bv. Ji nodl	3#1 alkB	tag	-HC		fius dnrV
30	Table 1 (c	Homologous gene				Agrobacterium tumefaciens celA	Saccharomyces cerevisiae				Pseudomonas aeruginosa rarD	Escherichia coli K12 vadS			Escherich a coli K12 abrB	Escherich a coli K12 vfcA			Escherichia coli K12 hrpB		Rhizobium feguminosarum bv. viciae plasmid pRL1JI nodL	Escherichia coli o373#1 alkB	Escherich'a coli K12 taq	Escherichia coli K12 rhtC	Bacillus subtilis yaaA	Streptomyces peucetius dnrV
<i>35</i>			+	<u> </u>	╁	₽¥.		+	$\vdash$		$\vdash$	T		$\vdash$	T		1	_		-		Esc	Esc	$\vdash$	1	
40		db Match				1451 pir 139714	1 sp.HKR1_YEAST				SP. RARD_PSEAE	Sp YADS ECOLI			SP. ABRB_ECOLI	SP. YFCA_ECOL			SP.HRPB_ECOLI		SP. NODL_RHILV	sp ALKB_ECOLI	Sp. 3MG1_ECOLI	Sp.RHTC_ECOL!	sp:YAAA_BACSU	prf.2510326B
		ORF (bp)	1941	1539	636	1451	1731	621	1065	756	879	717	333	1659	1137	798	624	405	2388	315	675	900	525	879	291	852
45		Terminal (nl)	138744	140329	139226	141789	143526	143075	144639	145480	145518	147239	147570	149780	149794	152369	150966	152814	153226	156167	156147	157537	158138	158831	159159	160013
50		Initial (nt)	136804	138791	139861	140329	141796	142455	143575	144725	146396	146522	147238	148122	150930	151572	151589	152410	155613	155853	156821	156848	157614	158154	.58869	159162
		SEQ NO.	3644	3645	3646	3647	3649	3649	3650	3651	3652	3653	3654	3655	3656	3657	3658	3659	3660	3661	3662	3663	3664	3665		3667
55	!	SEQ NO.	144	145	145	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161	162	163	Т		$\overline{}$	167

metabolite export pump of tetracenomycin C resistance

oxidoreductase

65.5

31.1

Bacillus subtilis yvaA

sp: vVAA\_BACSU

61.5

30.9

Streptomyces glaucescens tcmA

1374 sp.TCMA\_STRGA

SEC   Fig. 25   Fig. 26																						
SEC   Initial   Terminal ORF   Ab Match   Homologous gene   Genility Similarity Iength (a.s.)   (in)   (i			Function	nethyltransferase				bonuclease			leprilysin-like metallopeptidase 1		ranscriptional regulator, GntR family or fatty acyl-responsive regulator	ructokinase or carbohydrate kinase	sypothetical protein	nethylmalonic acid semialdehyde Jehydrogenase	nyo-inositol catabolism	myo-inositol catabolism	rhizopine catabolism protein	myo-inosital 2-dehydrogenase	myo-inositol catabolism	motabolite export numb of
SEC   Initial   Terminal   ORF   db Match   Homologous gene   (%)   (%)   (nt)   (nt)   (hp)   (hp	15		Matched length (a.a.)								Ī	:										
SEC   Initial   Terminal   ORF   db Match   Homologous gene   (%)   (%)   (nt)   (nt)   (hp)   (hp	20		Similarity (%)	56.7				76.3			57.2		65.6	63.0	2.08	1.38	58.2	8.69	51.0	72.2	72.1	
SEQ Initial Terminal ORF db Match (a.a.) (nl). (nl) (bp) db Match (a.a.) (nl). (nl) db Match (a.a.) (nl). (nl). (nl) db Match (a.a.) (nl).			Identity (%)	35.6				41.5			28.5		29.8	28.6	52.7	61.0	33.2	41.0	29.7	39.1	44.6	-
SEQ Initial Terminal ORF db Match (a.a.) (nl). (nl) (bp) db Match (a.a.) (nl). (nl) db Match (a.a.) (nl). (nl). (nl) db Match (a.a.) (nl).		1 (continued)	gous gene	omyces pombe c				ingitidis MC58			nl1		oli K12 farR		coelicolar A3(2)	coelicolor msdA	is iofB	Gloi si	eliloti mocC	is ich or iolG	is iofH	
SEQ Initial Terrinal ORF db Match (a a ) 3669 160029 160370 342 gp.SPAC1250_3 3669 160431 161360 930 3671 162295 161363 933 3672 162965 161363 933 3674 165737 166457 741 3675 165965 163899 2067 gp.AF176569_1 3676 166457 167419 963 3677 168595 167837 759 sp.FARR_ECOLI 3678 168975 167849 963 3679 169996 170916 921 gp.SC8F11_3 3680 170933 172444 1512 prt.2204281A 3681 172468 173355 888 sp.IOLB_BACSU 3683 175319 176272 954 sp.MOCC_RHIME 3683 175319 176272 954 sp.MOCC_RHIME 3684 176308 177318 1011 sp.MIZD_BACSU 3684 176308 177318 1011 sp.MIZD_BACSU	30	Table	Homolo	Schizosacchar SPAC 1250.04				Neissena men NMB0662			Mus musculus		Escherichia co	Beta vulgaris	Streptomyces SC8F11.03c	Streptomyces	Bacillus subtil	Bacillus subtil	Rhizobium m	Bacillus subti	Racillus subti	
SEQ Initial Terminal ORF NO. (nl) (nl) (nl) (hp) (a a) 3658 160029 160370 342 gas 567 161696 162352 657 3671 162965 163803 639 3672 162965 163809 2067 3674 165757 166457 741 3675 168955 1678991 1017 3678 169955 172444 1512 3681 172468 175319 176272 954 3683 175319 176272 954 3685 177334 176308 1011 3685 177334 176308 177334 176308 1011			db Match					:AE002420_13			3.AF176569_1		FARR_ECOLI	r: 14544	p:SC8F11_3	f.2204281A	PIOLE BACSU	PIOLD BACSU	MOCC BHIME	MIZD BACSU	IOI H BACSU	ביייים ויים
SEQ Initial Terminal (nl) (a a) (nl) (nl) (nl) (nl) (nl) (nl) (nl) (nl			ORF (bp)	<del></del>	930	657	933		639	741	1~	Ţ	i	1~	<b>+</b> -	7	_	. α	, [	ᡣ᠇	ے ا	2
SEQ NO. (aa) 3668 1 3668 1 3670 3676 3677 3676 3677 3676 3677 3676 3677 3680 3680 3680 3680 3680 3680 3680 3680	45			<del> </del>	-	-	i	<del> </del>	ì	166457	1	167419	167837	1	173916	172444	172355	175275	476272	17771R	178203	110203
	50		Initial (nl).	160029	160431	161696	162295	162463	162965	165717	165755	166457	168595	168975	169596	170933	172468	173548	475240	1_	1	
			SEQ NO.	3668	3659	L	3671	3672	3673	3674	3675	3676	3677	3678	3679	3680	7604	2695	•	· I	2000	3000
	55		SEO	168	169	170	171	172	173	174	175	176	111	178	179			ē [ Ş	70 5	20 20	5 5	 

							·																	
5 10		Function		redulatory protein	oxidoreductase	hypothetical protein		cold shock protein			caffeoyl-CoA 3-O-methyltransferase		glucose-resistance amylase regulator regulator	-		D-xylose proton symporter		transposase (ISCg2)	signal-transducing histidine kinase	glutamine 2-oxoglutarate aminolransferase large subunit	glutamine 2-oxogtutarate aminolransferase small subunit		hypothetical protein	
15		Matched length		331	442	303		64			134		338			458		401	145	1510	506		496	
20		Similarity (%)		619	52.5	64.7		92.2			58.2		62.1			70.5		100.C	60.7	100 0	8.66		72.8	
		Identity (%)		32.0	24.4	33.7		70.3			30.6		28.7			36.0		100.0	27.6	6.66	99.4		44.6	
30	Table 1 (continued)	Homo:ogous gene		Streptomyces reticuli cebR	Rhizobium sp. NGR234 y4hM	Bacillus subtifs yfiH		Streptomyces coelicolor A3(2) csp			Stellaria longipes		Bacillus subtilis ccpA			Lactobacillus brevis xylT		Corynebacterium glutamicum ATCC 13032 tnp	Rhizobium meliloti f.xl.	Corynebacterium glutamicum gltB	Corynebacterium glutamicum gltD		Mycobacterium tuberculosis H37Rv Rv3698	
40		db Match		gp:SRE9798_1	3 sp Y4HM RHISN	SP YFIH_BACSU		sp.CSP_ARTGO			prf.2*13413A		sp.ccPA_BACSU			Sp:XYLT_LACBR		gp:AF189147_1	Sp:FIXL_RHIME	gp:AB024708_1	gp:AB024708_2		pir:C70793	
		ORF (tp)	384	993	1233	1011	429	201	534	306	414	426	066	402	240	1473	300	1203	435	4530	1518	240	1485	369
45		Terminal (nt)	181647	181687	184051	185087	185642	186708	187302	187607	188100	188300	188747	190321	190389	190703	192949	194464	194604	199769	201289	201341	201760	205956
so		Initial (tc)	18:264	182679	182819	184077	185214	186508	186769	187302	3698 187687	188725	189736	189920	190628	192175	193248	193262	195038	195240	199772	201580	233244	205588
		SEQ NO.	3630	3691	3692	3633	3694!	3695	3696	3697	3698	3696	3700	3701	3702	3703	3704	3705	3706	3707	3708	3709		3711
55		NO (DNA)	198	191	192		194		8	197		8	200	201		:	204		202	207		509		211

EP 1 108 790 A2

10	Function	arabinosyl fransferase	alabinos), caracia	hypothetical membrane protein	acetoacetyl CoA reductase	oxidoreductasc				proteopnosphogiycan	hypothetical protein		hypothetical protein	rhamnosyl transferase		hypothetical protein	O-antigen export system ATP- binding protein	O-antigen export system permease protein	hypothetical protein	NADPH quinone oxidoreductase
15	Matched length (aa)	4422	7711	651	223	464				350	124		206	302		214	236	262	416	302
20	Similarity (%)	C	9.0/	66.1	56.5	85.1				57.4	83.9		73.8	79.1		55.1	78.4	75.6	63.0	71.5
	Identity (%)		39.8	35.0	31.4	0.09	·			24.3	60.5		43.2	63.6		31.3	47.0	31.3	36.5	41.1
25 Table 1 (continued)	us gene		ium embB	berculosis	phbB	berculosis				r ppg1	ıberculosis		berculosis	uberculosis fbE		imefaciens .URA tlorf100	olitica rfbE	olitica rfbD	luberculosis	ig3
So Table 1 ((	Homologous gene		Mycobacterium avium embB	Mycobacterium tuberculosis H37Rv Rv3792	Pseudomonas sp. phbB	Mycobacterium tuberculosis H37Rv Rv3790				Leishmania major ppg 1	Mycobacterium tuberculosis H37Rv Rv3789		Mycobacterium tuberculosis H37Rv Rv1864c	Mycobacterium tuberculosis H37Rv Rv3782 rfbE		Agrobacterium tumefaciens olasmid pTi-SAKURA tiorf100	Yersinia enterocolitica rfbE	Yersinia enterocolitica rfbD	Mycobacterium tuberculosis	Homo sapiens pig3
35				ΣI		ΣI				<b>,</b>	2		2 1.				<del> </del>	<del> </del>		1_6
40	db Match		prt:2224383C	pir.D70697	prf.2504279B	pir: B70697				gp:LMA243459	Sp: YOGN_MYCTU		pir:H70666	pir.870696		gp:AB016260_100	Sp. RFBE_YEREN	SP. RFBD_YEREN	pir.F70695	gp:AF010309_1
	ORF (bp)	318	3471	1583	759	1464	234	5:37	453	1002	396	402	633	939	342	297	799	804	1173	954
45	:erminal (nt)	206385	203541	207007	209210	209992	211535	212283	212735	213657	214107	214522	215159	215162	216605	216116	217141	217943	220151	220154
50	Initial (nt)	206068	207011	208589	209968	211455	211768	211777	212283	212656	213712	214121		216100	216264		217929	218746		221107
	SEO NO (a.a.)	3712	3713	3714	3715		3717	3718	3719	3720	3721	3722	3723	3724	3725	3726	3727			3730
55	SEQ NO.		Ť		215	216	217			220	221	222	223	224	225	226	227	228	229	230

		,		_															
5	Function		probable electron transfer protein	arrino acid carrier protein		mclybdopterin biosynthesis protein mceB (sulfurylase)	mclybdopterin synthase, large subunit	mclybdenum cofactor biosynthesis protein CB	co-factor synthesis protein	molybdopterin co-factor synthesis protein	hypothetical membrane protein	molybdate-binding periplasmic protein	molybdopterin converting factor subunit 1	maltose transport protein	hypothetical membrane protein	histidinol-phosphate aminotransferase			
15	Matched ength		92	475		368	150	158	154	377	227	256	96	355	121	330			
20	Simitarity (%)		51.0	75.8		70.1	75.3	63.3	84.4	58.6	5.07	0.89	70.8	8.09	76.9	65.8			
	Idertity (%)		35.0	46.7		43.8	44.7	33.5	61.7	34.5	44.1	34.0	37.5	34.3	36.4	37.3			
55 Table 1 (continued)	Homologous gene		Mycobacterium tuberculosis H37Rv Rv3571	Bacillus subtilis alsT		Synechococcus sp. PCC 7942 moeB	Arthrobacter nicotinoverans moaE	Synechococcus sp. PCC 7942 moaCB	Arthrobacter nicotinovorans moaC	Arthrobacter nicotinovorans moeA	Arthrobacter nicotinovorans modB	Arthrobacter nicolinovorans modA	Mycobacterium tuberculosis H37Rv moaD2	Thermococcus litoralis maik	Streptomyces coelicolor A3(2) ORF3	Zymomonas mobil:s hisC			
<i>35</i> 40	db Match		PIR:A70606	sp.ALST_BACSU		gs:SYPCCMOEB_	prf 2403296D	sp:MOCB_SYNP7	pf.2403296C	go:ANY10817_2	p-f.2403296F	рศ.2403296Е	pir:D70816	prf 2518354A	sp.YPT3_STRCO	sp.HISB_ZYMMO			
	CRF (bp)	582	297	1476	608	1083	456	471	466	1185	723	804	321	912	420	1023	906	294	120
45	Terminal (nt)	221131	222207	2222.0	225244	225242	226312	226760	227218	227703	229991	229711	230928	230931	231848	232260	234818	234910	235409
50	Initial (nt)	221712	221911	223685	224336	226324	226767	227230	227685	228887	229513	230514	230608	231842	232267	233282	233913	235203	235290
	SEQ NO (a.a.)	3731	3732	3733	3734	3735	3736	3737	3738	3739	3740	3741	3742	3743	3744	3745	3746	3747	3748
55	SEQ NO.	231	232	233	234	235	236	237	238	239	240	241	242	243	244	245	246		248

EP 1 108 790 A2

	_														- 1				_				$\neg \neg$	$\neg$	
5 10		Function	transcript on factor	alcohol dehydrogenase	pulrescine oxidase	magnesium ion transporter		Na/dicarboxylate cotransporter	oxidoreductase	hypothetical protein	nitrogen fixation protein			membrane transport protein	quauine (RNA-ribosyltransferase	hypothetical membrane protein	-		AEC transporter	glutamyl-tRNA synthetase		transposase			
15		Matched length (a.a.)	252 trans	335 alcol	451 putre	444 mag		567 Na/d	317 oxid	160 hypo	144 nitro				400 que	203 hyp				316 glut	_	360 tran			
20		Similarity M	57.1	0.99	38.1	68.5		59.6	69.1	73.8	70.1			45.7	0.89	62.1			49.6	63.3		55.0			
		identity (%)	29.4	340	215	30.9		332	46.1	48.8	45.1			20.7	41.3	28.1			24.3	34.8		34.2			
25	inued)	eue		philus	on	gtE			ulosis	ulosis	icum			culosis 22					scens strW			ae tnpA			
30	Table 1 (continued)	Homologous gene	Brucella abortus oxyR	Bacillus stearothermophilus DSM 2334 adh	Micrococcus rubens puo	Borrelia burgdorferi mgtE		Xenopus laevis	Mycobacterium tuberculosis H37Rv tyrA	Mycobacterium tuberculosis H37Rv Rv3753c	Bradyrhizobium japonicum			Mycobacterium tuberculosis H37Rv Rv0507 mmpL2	Zymomonas mobilis	Bacillus subtilis ypdP	,		Streptomyces glaucescens strW	Bacillus subtilis gltX		Pseudomonas syringae tnpA			
35 40		db Match	gp.BAU81286_1 E	15	Sp. PUO_M:CRU			prf.2320140A	pir.C70800	pir:B70800	gp:RHBNFXP_1			sp:YV34_MYCTU	SP.TGT_ZYMMO	sp:YPDP_BACSU			pr.S65588	sp:SYE_BACSU		gp:PSESTBCBAD_1			
		ORF (bp)	762   94	1017 sp	801	1350 pr	174	1530 pr		522 pi	417   91	201	351	2403 sı	1263 5	738 s	1030	648	1437 p	879 s	066	1110	303	138	
45		Terminal (nt)	235451	237342	238145	239525	239945	241515	241883	243431	243910	244215	244816	<del></del>	248572	248557	250507	249722	251939	252830	252830	254329	255492	255204	
5 <i>0</i>		Initial (nt)	236212	236326	237345	238176	239772	239986	242902	24291C	243494	244015	244466	244902	247310	249294	249428	250369	250503	251652	253819	255438	255794	256067	
		SEQ NO.	3749		3751	3752	3753	3754	3755	3756	3757	3758	3759	3760	3761	3762	3763	3764	3765	3766	3767	3768	3769	3776	
55		SEQ NO.	249	i	251	252	253	254	255	256	257	258	259	260	251	262	263	264	1 255	265	267	268	269	270	

5
10
15
20
25
30
35
40
45
50

SEC   Tritial   Termiral   CRF   db Match   Homologous gene   (%)   (%																	,—		_		
SEG   Tritial   Termiral   CRF   db Match   Homologous gene   (%)   (%		Function	aspartate transaminase		DNA polymerase III holoenzyme tau subunit		hypothetical protein	recombination protein	cotyric acid synthase	UDP-N-acetylmuramyl tripeptide synthetase	DNA polymerase III epsilon chain	hypothelical membrane protein	aspartate kinase alpha chain			extracytoplasmic function alternative sigma factor	vegetative catalase			leucine-responsive regulatory protein	branched-chain amino acid transport
SEC		Matched length (a a)	432				101	214	248	444	346	ļ .	421			189				143	203
SEO		Similarity (%)	100.0		53.1		74.3	72.4	61.7	9.09	55.2	100.0	8.66			63.5	76.4	-	-	72.0	68.0
SEQ "nitial Terminal ORF db Match (la b)		Identity (%)	98.6		31.6		41.6	42.5	38.3	31.3	25.7	100.0	99.5			31.2	52.9			37.1	30.5
SEQ 'nttal Terminal ORF db Match (la b) (nt) (lt) (ltp) (ltp) db Match (ltp) (nt) (ltp) (ltp) db Match (ltp) (nt) (ltp) (ltp) db Match (ltp) (ltp) (ltp) (ltp) db Match (ltp) (ltp) (ltp) (ltp) db Match (ltp)	Table 1 (continued)	Homologous gene	Brev bacterium lactofermentum aspC		Thermus thermophilus dnaX		Bacillus subtilis yaaK	Bacillus subtilis recR	Heliobacil us mobilis cobQ	Heliobacillus mobilis murC	Mycobacterium tuberculosis H37Rv dnaQ	Corynebacterium glutamicum (Brevibacterium flavum) ATCC 13032 orfX	Corynebacterium glutamicum lysC-alpha			Mycobacterium smegmatis sigE	Bacillus subtilis katA			Klebsiella pneumoniae Irp	Bacillus subtilis 1A1 azIC
SEO (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt)		db Match			gp:AF025391_1		sp:YAAK_BACSU	sp:RECR_BACSU	pri:2503462B			sp:YLEU_CORGL				prf.2312309A	sp.CATV_BACSU			Sp:LAP_KLEPN	753 sp.AZLC_BACSU
SEQ 'nitial Terminal ND (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt)		ORF (bp)	1296	630	2325	_	6CE	654	750	1269	1080	867	1263	1053	1434	579	1506	342	291		753
·····································		Terminal (nt)	257894	258529	260875	258596	261252	262055	262546	263298	264599	268258	270633	269524	_ ī	273542	275871	276232	275957	276302	27758:
·····································	!	initial (nt)	256599	257900	258551	259312		251402	253295	254566	265578	269124	269371	270576	271761	274120		275891	276247	276763	276829
		SEQ NO.	1778	3772	3773	3774	3775	3776	3777	3778	3779	3780	3781	3782	3783	3784	3785	3786	3787	3788	3.89
	! [	SEQ NO (DNA)	27.1	272	273	274	275	276	772	278	279	280	281	282	283	284	285	286	287	288	289

EP 1 108 790 A2

.10		Function			metalloregulatory protein	arsenic oxyanion-franslocation pump membrane subunit	arsenate reductase				Na+/H+ antiporter or multiple resistance and pH regulation related protein D	Na+/H+ antiporter	Na+/H+ antiporter or multiple resistance and pH regulation related protein A				transcriptional activator	two-component system sensor histidine kinase	alkaline phosphatase		phosphoesterase	hypothetical protein
15		Matched ength (aa)			06	341	119				503	119	824				223	521	180		307	149
<b>20</b>		Similarity (%)			68.9	84.2	689				70.4	9.07	64.3				70.4	56.8	0.09		54.7	71.8
		Identity (%)			34.4	52.2	31.1				32.4	37.0	34.1				38.6	26.7	28.3		26.1	37.6
25	Table 1 (continued)	Homologous gene			sp. As4 arsR	sp. As4 arsB	s xylosus arsC				OF4 mrpD	Staphylococcus aureus mnhC	ОЕ4 тгрА				trophus CH34	n tuberculosis	Lactococcus lactis MG1363 apl		s ykuE	s yqeY
30	Table	Homolo			Sinorhizobium sp.	Sinorhizobium sp. As4 arsB	Staphylococcus xylosus arsC				Baciilus firmus OF4 mrpD	Staphylococcu	Bacillus firmus OF4 mrpA				Alcaligenes eutrophus CH34 czcR	Mycobacterium tuberculosis mtrB	Lactococcus la		Bacillus subtilis ykuE	Bacillus subtilis yqeY
40	-	db Match			go:AF178758_1	gp:AF178758_2	sp.ARSC_STAXY				gp:AF097740_4	prf.2504285D	gp:AF097740_1				sp:CZCR_ALCEU	p4:2214304B	sp.APL_LACLA		p r.B69865	sp:YQEY_BACSU
		CRF (5p)	324	315	345 g	1380	387 s	318	270	753	1530 g	381	<del> </del>	1485	603	864	999	1467	693	561	915	453
45		Terminal (nt)	277904	277987	278388	279893	280279	280349	280670	280949	281404	282937	283317	287857	287059	287966	289131	289777	292417	291273	292597	293991
50		Initial (nt)	277581	278301	278732	278914	279993	280666	280939	281401	282933	283317		286373	287661	288829	289796	291243	291815	291833	293511	293539
		SEQ NO (a.a.)	3790	3791	3792	3793	3794	3795	3796	3797	3798	3799	3300	3801	3802	3803	3804	3805	3806	3807	3808	3805
55		SEQ NO (DNA)	290	231	292	293	294	295	296	297	298	589	300	301	302	303	. 36 1 45	305	306	327	308	309

5		Function	class A penicillin-binding protein(PBP1)	regulatory protein		hypothetical protein	transcriptional regulator	shikimate transport protein		long-chain-fatty-acid-CoA ligase	transcriptional regulator	3-oxoacyl-(acyl-carrier-protein) reductase	glutamine synthetase	short-chain acyl CoA oxidase	nodulation protein	hydrolase			cAMP receptor protein		ultraviolet N-glycosylase/AP lyase	cytochrome c biogenesis protein
15		Matched length (a.a.)	782	7.1		20	149	440		534	127	251	254	394	153	272			207		240	211
20		Similarity (%)	77.1	63.4		0.96	6.98	689		59.9	65.4	72.5	52.0	66.5	72.6	72.4			65.7		77.1	58.3
		Identity (%)	48.3	40.9		84.0	65.1	37.3		31.1	33.9	41.0	27.2	38.8	45.8	41.2			30.9		57.5	34.6
25	ntinued)	gene	ae pon 1	olor A3(2)		olor A3(2)	rculosis	shiA			olor A3(2)		luG	atg6	sarum nodN	rculosis					δρ	rculosis
30 35	Table 1 (continued)	Homologous gene	Mycobacterium leprae pon1	Streptomyces coelicolor A3(2) whiB		Streptomyces coelicolor A3(2) SCH-7.10c	Mycobacterium tuberculosis H37Rv Rv3678c	Escherichia coli K12 shiA		Bacillus subtilis IcfA	Streptomyces coelicolor A3(2) SCJ4.28c	Bacillus subtilis fabG	Emericella nidulans fluG	Arabidopsis thaliana atg6	Rhizobium leguminosarum nodN	Mycobacterium tuberculosis H37Rv Rv3677c			Vibrio cholerae crp		Micrococcus luteus pdg	Mycobacterium tuberculosis H37Rv Rv3673c
40		db Match	prf.2209359A	pir.S20912		gp:SCH17_10	pir.G70790	SP.SHIA_ECOLI		sp:LCFA_BACSU [	gp:SCJ4_28	sp:FABG_BACSU	SP.FLUG_EMENI	prf.2512386A	Sp:NODN_RHILV F	pir:F70790			prf:2323349A		sp:UVEN_MICLU	pir.B70790
		ORF (bp)	2385	339	192	153	459	1353	909	1536	525	633	945	194	47:	843	1173	705	681	192	780	558
45		Termina! (nt)	294034	297402	297622	297783	298250	298332	30008	299726	301512	303099	304074	305263	305758	306790	305195	307504	306782	307727	308734	309302
50		Initial (rt)	296388	297064	297431	297631	297792	299684	300087	301261	302036	302167	303133	304070	305288	305858	306367	3825 306800	307452	307918	3828: 307955	308745
	انتسر	SEQ NO. (a.a.)	3810	3811	3812	3313	3314	3315	3316	3917	3818	3819	3920	3821	3822	3823	3824	3825	3826	3827	3828	3829
55		SEQ NO (DNA)	310	311	312	313	314	315	316	317	318	319	320	321	322	323	324	325	326	327	328	329

EP 1 108 790 A2

			· ,								<del></del>			_			$\overline{}$				_
5		Function	hypothetical protein	serine proteinase	epoxide hydrolase	hypothetical membrane protein	phosphoserine phosphatase	hypothetical protein	conjugal transfer region protein		hypothetical membrane protein	hypothetical protein	hypothetical protein				ATP-dependent RNA helicase	cold shock protein		DNA topoisomerase 1	
15		Matched length (a.a.)	192	396	280	156	287	349	319	1	262	201	59				764	67		977	
20		Similarity (%)	56.3	71.0	52.1	77.6	65.5	60.2	66.5		63.7	64.2	84.8				66.1	88.1		81.6	
		identity (%)	30.7	38.6	29.6	46.8	29.6	35.0	32.9		30.5	33.8	47.5		-		33.8	68.7		61.7	
25 30	Table 1 (continued)	Homologous gene	ili K12 yeaB	n tubercu!osis ; c	Corynebacterium sp. C12 cEH	n tuberculosis 9	n leprae 2C. serB	Mycobacterium tuberculosis H37Rv Rv3660c	oli trbB		Mycobacterium tuberculosis H37Rv Rv3658c	Mycobacterium tuberculosis H37Rv Rv3657c	Mycobacterium tuberculosis H37Rv Rv3656c				is yprA	Arthrobacter g obiformis SI55 csp		Mycobacterium tuberculosis H37Rv Rv3646c topA	
35	Table	Homole	Escherichia coli K12 yeaB	Mycobacterium tuberculosis	Corynebacteri	Mycobacterium tuberculosis H37Rv Rv3669	Mycobacterium leprae MTCY20G9.32C. serB	Mycobacteriur H37Rv Rv366	Escherich:a coli trbB		Mycobacterium t H37Rv Rv3658c	Mycobacterium t H37Rv Rv3657c	Mycobacterium H37Rv Rv365	-			Bacillus subtilis yprA	Arthrobacter ( csp		Mycobacteriu H37Rv Rv364	
40		db Match	Sp. YEAB_ECOL	pir:H70789	prf:2411250A	pir:F70789	pir:S72914	pir.E70788	pir.C44020		pir.C7C788	pir:B70788	pir.A70788				sp:YPRA_BACSU	sp.CSP_ARTGO		pir:G70563	
		ORF (bp)	699	1191	993	549	396	1023	1023	615	816	546	198	318	414	345	2355	201	225	2988	711
45		Termina' (nt)	310038	311325	311899	312909	313625	316002	317132	316350	317893	318465	318689	319013	318545	319335	319336	322207	321992	325897	326614
50		Initial (nt)	309370	310135	312891	313457	314590	314980	316110	316964	317078	317920	318492	318596	318958	318991	321690	322007	322216	322910	325904
		SEQ NO	3830	3831	3832	3833	3834	3835	3836	3837	3839	3839	3840	3841	3842	3843	3844	3845	3846	3847	3848
55		SEQ NO.		331	332	333	334	335	336	337	338	339	340	341	342	343	344	345	346	347	348

5		tion		l subunit			_	bunit hase C	ylosidase		oendent drogenase		nase superfamily	rier-protein)	int protein	dehydratase		mannose		nthetase	ıse	
10		Function	adenylate cyclase	DNA polymerase III subunit tau/gamma		hypothetical protein	hypothetical protein	ribosomal large subunit pseudouridine synthase C	beta-glucosidase/xylosidase	beta-glucosidase	NAD/mycothiol-dependent formaldehyde dehydrogenase		metallo-beta-lactamase superfamily	3-oxoacyl-(acyl-carrier-protein) reductase	valanimycin resistant protein	dTDP-glucose 4,6-dehydratase	hypothetical protein	dolichol phosphate mannose synthase		nucleotide sugar synthetase	UDP-sugar hydrolase	
15 -		Matched length (a.a.)	263	423		144	172	314	558	101	362		160	251	415	320	108	230		260	586	
20		Similarity (%)	62.4	52.7		59.0	63.4	65.0	60.2	61.4	86.5		47.5	55.8	56.4	66.3	88.9	66.5		57.3	54.4	
		Identity (%)	32.7	25.3		32.6	39.0	43.6	34.8	38.6	9.99		32.5	25.9	26.3	33.8	59.3	33.9		25.8	26.1	
25	Table 1 (continued)	is gene	aca 817R23	аХ		dicum uu033	durans	12 rluC	eml D1 bgxA	ise salB	thano ica		ropolis orf5	12 fabG	ifaciens vImF	cbB	oerculosis	nnaschii JAL-		12 yefJ	urium ushA	
30	Table 1 (c	Homologous gene	Stigmatella aurantiaca B17R20 cyaB	Baci'lus subtilis dnaX		Ureaplasma urealyticum uu033	Deinococcus radiodurans DR0202	Escherichia coli K12 rluC	Erwinia chrysantheml D1 bgxA	Azospirilum irakense salB	Amycolatopsis methano ica		Rhodococcus erythropolis orf5	Escherichia coli K12 fabG	Streptomyces viridifaciens vlmF	Actinoplanes sp. acbB	Mycobacterium tuberculosis H37Rv Rv3632	Methanococcus jannaschii JAL- 1 MJ1222		Escherichia coli K12 yefJ	Salmonella typhimurium ushA	
35						3			<del> </del> -						_	¥	ΣÏ					
40		db Match	sp:CYAB_STIAU	sp.DP3X_BACSU		gp: AE002103	gp:AEC01882_8	sp:RLUC_ECOLI	Sp. BGLX_ERWCH	gp: AF090429_2	sp:FADH_AMYME		sp:YTH5_RHOSN	sp:FABG_ECOLI	gp:AF148322_	prf:2512357B	pir.A70562	sp:YC22_METJA		sp:YEFJ_ECOLI	YT⊒AS_AHSU.qs	
		ORF (bo)	1041	1257	162	444	561	882	1644	1989	1104	621	537	699	1230	933	375	759	1029	1035	2082	162
45		Terminal (nt)	326695	329539	329909	330376	331533	332433	334562	334953	336112	335185	336748	337449	338768	339725	340195	340559	342375	343451	345717	345814
50	į	Initial (nt)	327735	328283	329748	329933	330973	331552	332919	332965	335009	335805	336212	336781	337539	338793	340569	341327	341347	342417	343636	345975
		SEQ NO (8.8.)	3849	3850	3851	3852	3853	3854	3855	3856	3257	3958	3859	3860	3861	3862	3963	3864	3865	3966	3967	3868
55		SEO NO (DNA)	349	350	351	352	353	354	355	355	357	358	359	360	361	362	363	364	365	366	367	368

					,					<u> —</u> г				ſ	1						$\neg$		
5 10 		Function		NADP-dependent alcohol dehydrogenase	glucose-1-phosphate Ihymidylyllransferase	dTDP-4-keto-L-rhamnose reductase	dTDP-glucose 4,6-dehydratase	NADH dehydrogenase	Fe-regulated protein		hypothetical membrane protein	metallopeptidase	prolyl endopeptidase		hypothetical membrane protein	cell surface layer protein	autophosphorylating protein Tyr kinase	protein phosphatase		caosular polysaccharide biosynthesis	ORF 3	I popolysaccharide biosynthesis / aminotransferase	
15		Matched length (a.a.)		343	285	192	343	206	325		423	461	708		258	363	453	102		613	06	394	
20		Similarity (%)		74.9	84.9	74.0	83.4	61.2	66.5		683	62.5	56.4		46.0	76.6	57.2	9.89		65.7	51.0	68.3	
		Identity (%)		52.2	62.8	49.5	61.8	35.4	33.2		37.4	34.1	28.4		26.0	50.7	28.5	39.2		33.0	41.0	37.1	l I
25	Table 1 (continued)	is gene		serculosis	n M32 rfbA	lans milC	tans XC rmlB	s HB8 nox	reus sirA		perculosis	licolor	psulata		licolor A3(2)	rcc 6872	Isorii ptk	sonii ptp		ureus M capD		uni wlaK	
30	Table 1	Homologous gene		Mycobacterium tuberculosis H37Rv adhC	Salmonella anatum M32 rfbA	Streptococcus mutans milC	Streptococcus mutans XC rmlB	Thermus aquaticus HB8 nox	Staphylococcus aureus sirA		Mycobacterium tuberculosis H37Rv Rv3630	Streptomyces coelicolor SC5F2A.19c	Sphingomonas capsulata		Streptomyces coelicolor A3(2)	Corynebacterium ammoniagenes ATCC 6872	Acinetobacter johnsorii ptk	Acinetobacter johnsonii ptp		Staphylococcus aureus M capD	Vibrio cholerae	Campylobacter jejuni wlaK	
35			•	<u>₹</u> 9	Sa	क्र	$\vdash$	F	š	_	ΣÏ	# S	တ်		ऊ	ರ ಕ	¥	¥	_		=	<u> </u>	
40		db Match		sp:ADH_MYCTU	sp:RFBA_SALAN	gp:D78182_5	Sp.RM.B_STRWU	Sp NOX_THETH	prf:2510361A		sp:v17M_MYCTU	gp:SC5F2A_19	prf.2502226A		gp:SCF43_2	gsp W56 155	prf:2404346B	prf:2404346A		sp:CAPD_STAAU	PRF:2109288X	prf.2423410L	
		OR? (bp)	351	1059	855	1359	1131	579	945	639	1308	1380	2118	573	.092	1095	1434	603	984	1812	942	1155	
45		Terminal (nt)	346110	346961	348098	348952	350313	351370	353637	353749	354599	355849	357237	359762	360814	362057	365257	365852	366838	368643	367701	369801	
50		Initial (nt)	346460	346019	348952	350310	351443	351948	352693	354387	355906	357228	359354	360334	361905	363151	363824	365250		366832	368642	368647	
	بمسر	SEQ NO (a.a.)	3869	3870	3871	3872	3873	3874	3875	3876	3877	3878	3879	3880	3881	3882	3883	3884	3885	3885	3887	3888	
55		SEQ NO (DNA)		370	37.1	372	373	374	375	376	377	378	379	380	381	382	383	384	<del>i -</del>	386	387	1	

5	
10	
15	
20	
25	
30	
<b>35</b>	
40	
45	
50	

Table 1 (continued)

	T	1	1		T	_	_~		<del></del>	1		т		<del></del> -		_	_	1	
Function	pilin glycosylation protein	capsular polysaccharide biosynthesis	Ipopolysaccharide biosynthesis / export protein	UDP-N-acetylglucosamine 1- carboxyviny:transferase	UDP-N- acetylenolpyruvoylglucosamine reductase	sugar transferase	transposase		fransposase (insertion sequence IS31831)		hypothetical protein	acetyltransferase	hypothetical protein B	UDP-glucose 6-dehydrogenase			glycosyl transferase	acetyltransferase	
Matched length (a.a.)	196	380	504	427	273	356	53		70		404	354	65	388			243	221	
Similarity (%)	75.0	69.2	69.8	64.6	68.5	57.3	79.3		94.3		57.4	60.2	53.0	89.7			65.0	62.0	
Identity (%)	54.6	33.4	34.3	31.4	34.8	32.0	60.4		75.7		28.0	34.5	44.0	63.7			32.1	33.0	
Homologous gene	Neisseria meningitidis pgIB	Staphylococcus aureus M capM	Xanthornonas campestris gumJ	Enterobacter cloacae murA	Bacillus subtilis murB	Vibrio cholerae ORF39x2	Corynebacterium glutamicum		Corynebacterium glutamicum ATCC 31831		Mycobacterium tuberculosis H37Rv Rv1565c	Pseudomonas aeruginosa PAO1 psbC	Corynebacterium glutamicum	Escherichia coli ugd			Escherichia coli wbnA	Escherichia coli 0157 w5h11	
db Match	gp:AF014804_1	sp.CAPM_STAAU	pir:S67859	sp MURA_ENTC:	sp:MURB_BACSU	gp:VCLPSS_9	prf:2211295A		pir:S43613		pir.G70539	gsp.W37352	PIR: S60890	sp:UDG8_ECOLI			gp:AF172324_3	gp:AB036676_13	
(tp)	612	1161	:491	1314	500.	.035	150	135	327	276	1170	993	231	1161	273	1209	822	645	195
Terminal (nt)	370405	371773	373419	374813	375837	376876	377832	378227	378511	378287	378668	379850	381495	383108	383496	383982	385374	387200	387463
Initia' (nt)	369794	370613	371929	373500	374833	375842	377683	378093	378185	378562	379837	3900 380842	381265	381948	383769	385190	386195	386556	387557
SEQ NO (a.a.)	3889	3890	3891	3892	3893	3894	3895	3896	3897	3898	3899	3900	3901	3902	3903	3904	3905	9060	3907
SEQ NO.	389	390	39.1	392	393	394	395	396	397	398	399	400	401	402	403	404	405	406	407

EP 1 108 790 A2

5	Function	dihydrolipoamide dehydrogenase	UTP-glucose-1-phosphate uridylyltransferase	otein	al regulator	b subunit	succinate dehydrogenase flavoprotein	succinate dehydrogenase subunit B						protein	protein			tetracenomycin C transcription repressor		
10		dihydrolipoar	UTP-glucose-1-pt uridylyltransferase	regulatory prote <sup>i</sup> n	transcriptional regulator	cytochrome b subunit	succinate de flavoprotein	succinate de						hypothetical protein	hypothetical protein			tetracenomy repressor		transporter
15	Matched length (a.a.)	469	295	153	477	230	608	258						259	431			197		499
20	Similarity (%)	100.0	68.1	71.9	81.3	67.4	61.2	56.2						49.8	64.3			53.8		74.6
	Identity (%)	99.6	41.7	43.8	57.0	34.8	32.4	27.5						26.3	32.7			26.4		36.1
25 (panuju	gene	tamicum	estris	inosa PAO1	rculosis	olor A3(2)	1	ans sdhB						olor	yjiN			scens		e T#2717
ss on Table 1 (continued)	Homologous gene	Corynebacterium glutamicum ATCC 13032 lpd	Xanthomonas campestris	Pseudomonas aeruginosa PAO1 ortX	Mycobacterium tuberculosis H37Rv Rv0465c	Streptomyces coelicolor A3(2) SCM10.12c	Bacillus subtilis sdhA	Paenibacillus macerans sdhB						Streptomyces coelicolor SCC78.05	Escherichia coli K12 yjiN			Streptomyces glaucescens GLA.0 tcmR		Streptomyces fradiae T#2717 urdJ
40	db Match	gp:CGLPD_1	pir.JC4985	gp:PAU49666_2	pir.E70828	gp:SCM10_12	pir.A27763	gp.BMSDHCAB_4			,			gp:SCC78_5	sp:YJIN_ECOLI			sp:TCMR_STRGA		gp:AF164961_8
	ORF (bp)	1407	921	498	1422	77:	1875	837	336	261	630	96	339	975	1251	420	303	829	204	1647
45	Terminal (nt)	389098	390168	390730	390787	393475	395513	396262	396650	396932	396411	397825	398222	397232	399579	400017	400341	401150	401253	402796
50	Initial (nt)	387692	389248	390233	3911 392208	392705	393639	395426	396315	396672	397040	397730	397884	398206	398329	399598	400039	400473	401050	401:50
	SEQ NO (a a.)	3908	3909	3910	3911	3912	3913	3914	3915	3916	3917	3918	3919	3920	3921	3922	3923	3924	3925	3925
55	SEQ NO.	408	409	410	411	412	413	414	415	416	417	418	419	420	421	422	423	424	425	426

5		Function	Iransporter	formyltetrahydrofolate deformylase	deoxyribose-phosphate aldolase			hypothetical protein	hypothetical protein		cation-transporting P-type ATPase B		glucan 1,4-alpha-glucosidase	hemin-binding periplasmic protein	ABC transporter	ABC transporter ATP-binding protein	hypothetical protein	hypothetical protein			
15		Matched length (a.a.)	<del>                                     </del>	286 (	1			280 h	92 h		748 c		626 g	348 h	330	254 A	266 h	258 h	:		
20		Similarity (%)	74.6	72.7	74.0			53.6	85.9		75.3		56.1	83.6	90.3	85.0	56.4	61.6	:		
		Identity (%)	39.6	40.9	38.5			26.8	58.7		45.7		27.3	57.2	65.2	63.8	28.6	32.6			
25	ntinued)	gene	9 T#2717	P-1 purt:				n GIR 10	culosis		e ctpB		visiae	htheriae	htheriae	htheriae	lor C75A	lor C75A			
30	Table 1 (continued)	Homologous gene	Streptomyces fradiae T#2717 urdJ	Corynebacterium sp. P-1 purU	Bacillus subtilis deoC			Mycobacterium avium GIR10 mav346	Mycobacterium tuberculosis H37Rv Rv0190		Mycobacterium leprae ctpB		Saccharomyces cerevisiae S288C YIR019C sta1	Corynebacterium diphtheriae hmuT	Corynebacterium diphtheriae hmuU	Corynebacterium diphtheriae hmuV	Streptomyces coelicolor C75A SCC75A.17c	Streptomyces coelicolor C75A SCC75A.17c			
35			SE	_	r		-	ΣE	Σĭ	_	_			ŭΞ	ŏΞ	ŏΞ	တ် လ	တ် လ	-	_	H
40		db Match	gp AF164961_8	sp:PURU_CORSP	sp.DEOC_BACSU			prf.2413441K	pir.A70907		Sp:CTPB_MYCLE		SP. AMYH_YEAST	gp:AF109162_1	gp:AF109162_2	gp:AF109162_3	gp:SCC75A_17	gp:SCC75A_17			
		ORF (bp.)	1632	912	999	150	897	867	300	900	2265	450	1863	1077	, C68	813	957	837	810	813	501
45		Terminal (nt)	404430	404508	406145	406161	405521	407416	407409	409145	40?711	410027	412545	413633	414710	415526	416599	417439	417545	418441	419257
50		Initial (nt)	402799	405419	405480	406310	406417	406550	407708	408546	405975	3936   410476	410683	3938 412557	3939 413643	414714	415643	416603	418354	419253	419757
		SEQ NO (a a)	3927	3928	3929	3930	3931	3932	3933	3934	3935	3936	3937	3938	3939	3940	3941	3942	3943	3944	3945
55	:	SEQ NO NO NO	427	428	429	430	431	432	433	434	435	436	437	438	439	440	441	442	443	444	445

	1							1	Т			Ŧ	<u>.</u>		<u> </u>			丁		$\neg$
5		Function	UDP-N-acetylpyruvoylglucosamine reductase				long-chain-fatty-acidCoA ligase	transferase	phosphoglycerate mutase	two-component system sensor histidine kinase	two-component response regulator		ABC transporter ATP-binding protein	cytochrome P450	exopolyphosphatase	hypothetical membrane protein	pyr:oline-5-carboxylate reductase	membrane glycoprotein	hypothetical protein	
			UDP				long	trans	bhos	histic	φ.		ABC	cyto	exo	hypc	pyr	men	hyp (	
15		Matched length (a.a.)	356				558	416	246	417	231		921	269	306	302	269	394	55	
20		Similarity (%)	58.4				68.1	58.7	84.2	74.8	6.06		60.7	6.99	57.8	57.3	100.0	52.0	94.6	
		identity (%)	30.1				35.5	33.9	70.7	49.2	75.8		31.3	45.0	28.8	28.8	100.0	25.4	76.4	
25	(panu	90	12 murB					_	ır A3(2)	enX3	SCG		or A3(2)	ulosis	osa ppx	utosis	ımicum	ORF71		
30	Table 1 (continued)	Homologous gene	Escherichia coli RDD012 mu:B				Bacillus subtilis IcfA	Streptomyces coelicolor SC2G5.06	Streptomyces coelicolor A3(2) gpm.	Mycobacterium bovis senX3	Mycobacterium bovis BCG regX3		Streptomyces coelicolor A3(2) SCE25.30	Mycobacterium tuberculosis H37Rv RV3121	Pseudomonas aeruginosa ppx	Mycobacterium tuberculosis H37Rv Rv0497	Corynebacter um glutamicum ATCC 17965 proC	Equine herpesvirus 1 ORF71	Mycobacterium leprae B2168_C1_172	
35		·	<del>                                     </del>			!		SS			2. 5		0) 0)		ū		<u> </u>		2. 0	
40		db Match	gp:ECOMURBA_1				SP:LCFA_BACSU	gp.SC2G5_6	sp.PMGY_STRCO	prf 2404434A	prf.2404434B		gp SCE25_30	sp:YV21_MYCTU	prf.2512277A	sp:YV23_MYCTU	sp.PROC_CORGL	gp D88733_1	pir S72921	
		ORF (bp)	1101	651	735	174	1704	1254	744	1239	969	879	2586	903	927	813	810	1122	198	219
45		Terminal (nt)	420885	421516	42C309	422031	422090	425131	425920	427172	427867	429439	429438	432126	433988	434822	435695	433865	436137	436103
50		Initial (nt)	419785	420866	421043	421858	423793	423878	425177	425934	427172	428561	432023	433028	433062	434910	434886	434986	435940	436321
		SEQ NO	<del></del>	3947	3948	3949	3950	3951	3952	3953	3954	3955	3955	3957	3958	3959	3960	3961	3962	3963
55		SEO ON (AND)	+	447	448	449	450	451	452	453	454	455	455	457	458	459	460	46:	462	463
		!	· · · · · · · · · · · · · · · · · · ·	<u> </u>		<del>!</del>	<b></b>	<u> </u>	<u> </u>	1	<u> </u>	.l	·	.i	<u>:</u>	4		<del></del> .	• • • •	÷

									,			,				,		,		,			
5		Function	ırotein			phosphoserine phosphatase	rotein		\ reductase	hydroxymethylbilane synthase		cat operon transcriptional regulator	sport protein	3-dehydroshikimate dehydratase	ydrogenase		nsport protein		iron(III)-transport system permease protein		periplasmic-iron-binding protein	uroporphyrin-III C-methyltransferase	
10			hypothetical protein			phosphoserin	hypothetical protein		glutamyl-tRNA reductase	hydroxymethy		cat operon tra	shikimate transport protein	3-dehydroshik	shikimate dehydrogenase		putrescine transport protein		iron(III)-transp protein		periplasmic-iro	croporphyrin-l	
15		Matched length: (a.a.)	29			296	74		455	308		321	417	309	282		363		878		347	486	
20		Similarity (%)	100 C			77.4	66.2		74.3	75.3		57.6	72.2	57.9	98.6		9.89		55.2		59.9	71.6	
		Identity (%)	89.7			51.0	40.5		44.4	50.7		17.1	35.5	282	98.2		34.7		25.1		25.1	46.5	
25	Table 1 (continued)	eueb sı	color			orae serB	perculosis		rae hemA	rae hem3b		oaceticus	2 shiA	1 qa4	jutamicum		12 potG		ns sfuB		senteriae bitA	rae cysG	
30 35	Table 1 (c	Homologous gene	Streptomyces coel·color SCE68.25c			Mycobacterium leprae MTCY20G9.32C. se:B	Mycobacterium tuberculosis H37Rv Rv0508		Mycobacterium leprae hemA	Mycobacterium leprae hem3b		Acinetobacter calcoaceticus catiV	Escherichia coli K12 shiA	Neurospora crassa qa4	Corynebacterium glutamicum ASO19 aroE		Escherichia coli K12 potG		Serratia marcescens sfuB		Brachyspira hyodysenteriae bitA	Mycobacterium leprae cysG	
40		db Match	gp:SCE68_25			pi: S72914	sp:YV35_MYCTU		Sp:HEM1_MYCLE	pir.S72887		Sp.CATM_ACICA	sp:SH.A_ECOLI	sp.3SHD_NEUCR	gp:AF124518_2		sp.POTG_ECOLI		sp:SFUB_SERMA		gp.SHU75349_1		
		ORF (bp)	66	192	618	1065	246	258	1389	906	372	882	1401	1854	849	273	1050	615	1644	1113	1059	1770	426
45		Terminal (nt)	436561	436764	437850	436980	438424	438037	439904	440814	441591	441501	444158	446038	447386	447398	448130	449100	449183	451961	450837	454430	454875
50		initial (nl)	435463	436573	437233	438044	438179	438294	438516	433909	441220	442482	442758	444.85	446538	447670	449179	449714	450826	450849	451895	452661	454450
		SEQ NO (a a)	3964	3965	3966	3965	3968	3969	3970	3971	3972	3973	3974	3975	3976	3977	3978	3979	3980	3981	3982	3983	3984
55		SEO SO SEO	464	465	466	467	468	469	470	471	472	473	474	475	476	477	478	479	480	481	482	483	484

		$\overline{}$																			
. 5		Function	delta-aminolevulinic acid dehydratase			cation-transporting P-type ATPase B		uroporphyrinogen decarboxylase	protoporphyrinogen IX oxidase	glutamate-1-semialdehyde 2,1- aminomutase	phosphoglycerate mutase	hypothetical protein	cytochrome c-type biogenesis protein	hypothetical membrane protein	cytochrome c biogenesis protein		franscriptional regulator	Zn/Co transport repressor		typothetical membrane protein	1,4-dihydroxy-2-naphthoate cctaprenytransferase
15		Matched length (a.a.)	337			858		364	464	425	161	208	245	533	338		144	96		82	301
20		Similarity (%)	83.1			56.5		76.7	59.9	83.5	32.7	71.2	35.3	76.0	17.8		69.4	72.2		78.1	61.5
		Identity (%)	8.09			27.4		55.0	28.0	61.7	28.0	44.7	53.5	50.7	44.1		38.9	31.1		39.0	33.6
25	Table 1 (continued)	us gene	licolor A3(2)			prae ctpB		licolor A3(2)	ım.Y	prae heml.	12 gpmB	berculosis	berculosis	berculosis	berculosis		berculosis 165	ureus zntR		berculosis	12 menA
30	Table 1 (	Homologous gene	Streptomyces coelicolor A3(2) hemB			Mycobacterium leprae ctpB		Streptomyces coelicolor A3(2) hemE	Bacillus subtilis hemY	Nycobacterium leprae heml.	Escherichia co i K12 gpmB	Mycobacterium tuberculosis H37Rv Rv3526	Mycobacterium tuberculosis H37Rv ccsA	Mycobacterium tuberculosis H37Rv Rv0528	Mycobacterium tuberculosis H37Rv ccsB		Mycobacterium tuberculosis H37Rv Rv3678c pb5	Staphylococcus aureus zntR		Mycobacterium tuberculosis H37Rv २v0531	Escherichia col <sup>:</sup> K12 menA
35		atch	_			MYCLE															
40		db Match	sp.HEMZ_STRCO			sp:CTPB		sp:DCUP_STRCO	sp:PPOX_BACSU	sp:GSA_MYCLE	sp.PNG2_ECOLI	pir.A70545	pir:870545	pir.C70545	pir:D70545		pir.G73790	prf:2420312A		pir.F70545	sp WENA_ECOL!
		ORF (bp)	1017	582	510	2544	843	1074	1344	1311	909	621	792	1623	1011	801	471	357	300	333	854
45		Terminal (nt)	455983	456597	457150	459900	458583	461093	462455	463867	464472	465102	465909	467571	468658	470170	470654	470657	471121	471847	471915
50		In tial (nt)	454967	456016	456641	457357	459425	46C023	461112	462557	463867	464482	465118	465949	467648	469370	470184	471013	471420	471515	472808
		SEQ NO. (a a)	3985	3986	3987	3988	3989	3950	3991	3992	3993	3994	3995	3596	3997	3998	3999	4000	4001	4005	4003
55		SEO NO (DNA)	485	486	487	488	489	490	491	492	493	494	495	496	497	498	499	500	501	502	503

pterin-4a-carbinolamine dehydratase

68.8 82.7

muconate cycloisomerase

335 11

76.7

54.0 37.7

Mycobacterium tuberculosis H37Rv Rv0553 menC Aquifex aeolicus VF5 phhB

1014 pir.D70548

487014 485077

4022

pir C70304

309

485385 486001

4021

		_	7			r				_		$\overline{}$	•		_	_	-	
5	Function	83	rboxylase	rane protein	aldehyce	glucarate	ny protein			ooxylic acid				ic phosphate			95	
10	Func	glycosyl transferase	maionyl-CoA-decarboxylase	hypothetical membrane protein	ketoglutarate semialdehyce dehydrogenase	5-dehydro-4-deoxyglucarate dehydratase	als operon regulatory protein	hypothetical protein		2-pyrone-4,6-dicarboxylic acid				low-affinity inorganic phosphate transporter			naphthoate synthase	peptidase E
15	Matched length (a.a.)	238	421	139	520	303	293	46		267	T			410			293	202
20	Identity Similarity (%)	62.6	51.5	65.5	76.0	75.6	66.2	64.9		54.7				83.2			703	82.7
	Identity (%)	32.4	25.4	35.3	50.4	48.5	36.9	33.0		28.1				9.09			48.5	57.9
25 (penuji	Jene	cgB	B	γqiF		нсвах	IsR	culosis		126 fldB				culosis				ans
20 Table 1 (continued)	Homologous gene	Bacteroides fragilis wcgB	Rhizobium trifolii matB	Escherichia coli K12 yqiF	Pseudomonas pulida	Pseudomonas putida KDGDH	Bacillus subtilis 168 alsR	Mycobacterium tuberculosis H37Rv Rv0543c		Sphingomonas sp. LB126 fldB				Mycobacterium tuberculosis H37Rv pitA			Bacillus subtilis menB	Deinococcus radiodurans DR1070
40	cb Match	gp:AF125164_6	prf 242327CB	sp.YQJF_ECOLI	pir:S27612	sp:KDGD_PSEPU	sp:ALSR_BACSU	pir:870547		gp:SS>277235_9				pir:D70547			Sp:MENB_BACSU	9p:AE001957_12 [
	ORF (bp)	864	1323	411	1560	940	879	315	444	097	417	378	261	1275	222	306	957	603
45	Terminal (nt)	473811	473914	474997	475489	477048	478092	478989	480597	479452	480208	480624	481131	481394	483366	483637	484106	485986
50	Initial (nt)	472948	475136	475407	477048	477995	478970	479303	480154	4802C1	480624	48.001	481391	482668	483587	483942	485062	
	SEQ NO.	4004	4005	4006	4007	4008	4009	4010	4011	4012	4013	4014	4015	4016	4017	4018	4019	4020
55	SEQ NO (DNA)	504	505	206	205	208	209	510	511	512	513	514	515	516	517	518	519	920

EP 1 108 790 A2

	Function	2-oxoglutarate decarboxylase and 2 succinyl-6-hydroxy-2,4-cyclohexadiene-1-carboxylate synthase	hypothelical membrane protein	alpha-D-mannose-alpha(1- 6)phosphatidyl myo-inositol monomannoside transferase	D-serine/D-alanine/glycine transporter	ubiquinone/menaquinone biosynthesis methyltransferase		oxidoreductase	heptaprenyl diphosphate synthase component II	preprotein translocase SecE subunit	transcriptional antiterminator protein	50S ribosomal protein L11	50S ribosomal protein L1	regulatory protein	4-aminobutyrate aminotransferase	
ļ	Matched length (a.a.)	909	148	408	447	237		412	316	111	318	145	236	564	443	
	Identity   Similarity (%)	54.0	64.9	54.2	89.9	66.7		76.7	67.1	100.0	100.0	100.0	100.0	50.2	82.4	
	Identity (%)	29.4	37.2	22.8	66.2	37.1		49.0	39.2	100.0	100 0	100.0	100.0	23.1	60.5	
Table 1 (continued)	Homologous gene	Bacillus subtilis menD	Mycobacterium tuberculosis H37Rv Rv0556	Mycobacterium tuberculosis H37Rv pimB	Escherichia coli K12 cycA	Escherichia coli K12 ubiE		Mycobacterium tuberculosis H37Rv Rv0561c	Bacillus stearothermophilus ATCC 10149 hepT	Corynebacterium glutamicum ATCC 13032 secE	Corynebacterium glutamicum ATCC 13032 nusG	Corynebacterium glutamicum ATCC 13032 rolK	Corynebacterium glutamicum ATCC 13032 rpIA	Streptomyces coelicolor SC5H4.02	Mycobacterium tuberculosis H37Rv RV2589 gabT	
	db Match	sp:MEND_BACSU	pir.G70548	239 pir.H70548	sp:CYCA_ECOLI	sp:UBIE_ECCLI		pir.D70549	050 sp:HEP2_BACST	gp:AF130462_2	gp:AF130462_3	gp.AF130462_4	gp:AF130462_5	gp.SC5H4_2	sp:GABT_MYCTU	
	ORF (bp)	1629	441	1239	1359	069	699	1272	1050	333	954	435	708	1512	1344	
	Terminal (nt)	488656	489100	490447	491938	492655	493583	492645	495110	497142	498327	499032	499869	499925	522920	
	Initial (nt)	487028	468660	489209	490580	491965	492915	493916	494061	495810	4032 497374	493598	499162	501436	501577	
	SEQ NO (a.a.)	4023	4024	4025	4026	4027	4028	4229	4030	4031	4032	4033	4034	4035	4036	
	SEQ NO (DNA)	523	524	525	526	527	528	529	530	531	532	533	534	535	536	

			<del>-,</del> -																
5		Function	succinate-semialdehyde dehydrogenase (NAD(P)+)	novel two-component regulatory system	lyrosine-specific transport protein	callon-transporting ATPase G	hypothetical protein or	5010	50S ribosomal protein L10	50S ribosomal protein L7/L12		hypothetical membrane protein	DNA-directed RNA polymerase beta chain	DNA-directed RNA polymerase beta chain	hypothetical protein		DNA-binding protein	al protein	
			succinate	novel two	tyrosine	cation-tra	hypothetical pro	Solo (III)	50S ribos	50S ribos		hypothetic	DNA-direc	DNA-direc	hypothetic		DNA-bind	hypothetical protein	
15		Matched , length (a.a.)	461	150	447	615	468		170	130		283	1180	1332	169		232	215	
20		Similarity (%)	71.8	38.0	49.9	64.4	66.2		84.7	89.2		55.5	90.4	88.7	52.0		63.8	57.7	
		identity (%)	40.8	32.0	25.5	33.2	40.2		52.9	72.3		25.8	75.4	72.9	39.0		39.2	29.3	
25	Table 1 (continued)	us gene	.12 gabD	lense carR	12 0341#7	berculosis ctoG	lans P49		eus N2-3-11	bercutosis IL		berculosis	berculosis oB	serculosis cC	oerculosis .		icolor A3(2)	erculosis	
30	Table 1 (	Homologous gene	Escherichia coli K12 gabD	Azospirillum brasilense carR	Escherichia coli K12 o341#7 tyrP	Mycobacterium tuberculosis H37Rv RV1992C ctpG	Streptomyces lividans P49		Streptomyces griseus N2-3-11	Mycobacterium tuberculosis H37Rv RV0652 rplL		Mycobacterium tuberculosis H37Rv Rv0227c	Mycobacterium tuberculosis H37Rv RV0667 rpoB	Mycobacterium tuberculosis H37Rv RV0668 rpcC	Mycobacterium tuberculosis H37Rv Jv0166c		Streptomyces coelicolor A3(2) SCJ9A. 15c	Mycobacterium tuberculosis H37Rv RV29C8C	
<i>35</i> 40		db Malch	sp.GABD_ECOLI	GP. ABCARRA_2	Sp.TYRP_ECOLI	sp.CTPG_MYCTU	Sp P49_STRLI		sp.RL1C_STRGR	sp RL7_MYCTU		p r A70962	sp.RPOB_MYCTU	sp:RPOC_MYCTU	GP.AF12:004_1		gp:SCJ9A_15	SP:YT38_MYCTU	
		ORF (bp)	1359	468	1191	1950 s	1413 s	503	513	384 s	138	972 p	3495 s	3999 8	582 G	180	780 91	ls: 66/	
45		Terminal (nt)	504283	503272	505569	507647	509081	509696	510510	510974	510989	512507	516407	520492	518696	520850	521644	521679	
50		nitial (nt)	502925	503739	504379	505698	507669	509094	509998	5:0591	5.1126	511536	512913	516494	519277	520671	520855	522476	
		SEQ NO (a.a.)	4037	4038	4039	4040	4041	4042	4043	4044	4045	1046	4047	4048	4049	4050	405:	4352	
55	-	SEQ NO (DNA)	537	538	539	540	541	542	543	544	545	546	547	548	549	550	551	552	

EP 1 108 790 A2

	-					_	_	_	_														_
5		Function	30S ribosomal protein S12	30S ribosomal protein S7	elongation factor G			lipoprotein			ferric enterobactin transport ATP- binding protein	ferric enterobactin transport protein	ferric enterobactin transport protein	butyryl-CoA acetate coenzyme A transferase	30S ribosomal protein S10	50S ribosomal protein L3		50S ribosomal protein L4	50S ribosomal protein L23		50S ribosomal protein L2	30S ribosomal protein S19	
15		Matched length (a.a.)	121	154	709			44			258	329	335	145	101	212		212	98		280	92	
20		Similarity (%)	97.5	94.8	88.9			78.0			83.7	8.77	90.6	79.3	99.0	9.68		90.1	9.06		92.9	98.9	
		Identity · (%)	90.9	81.8	71.7			56.0			56.2	45.6	48.1	58.6	84.2	99	-	71.2	74.0		80.7	87.0	
	Table 1 (continued)	Homologous gene	Mycobacterium intracellulare rpsL	Mycobacterium smegmatis LR222 rpsG	Micrococcus luteus fusA			Chlamydia trachomatis			Escherichia coli K12 fepC	Escherichia coli K12 fepG	Escherichia coli K12 fepD	Thermoanaerobacterium thermosaccharolyticum actA	Planobispora rosea ATCC 53733 rpsJ	Mycobacterium bovis BCG rplC		Mycobacterium bovis BCG rplD	Mycobacterium bovis BCG rpfW		Mycobacterium bovis BCG rplB	Mycobacterium tuberculosis H37Rv RvC705 rpsS	
40		db Match	sp.3S12_MYCIT	sp-3S7_MYCSM	sp.EFG_MICLU			GSP:Y37841			Sp.FEPC_ECOU	SP:FEPG_ECOU	SP FEPD_ECOU	gp:CTACTAGEN_1	sp:RS10_PLARO	sp: RL3_MYCBO		Sp. RL4_MYCBO	sp.RL23_MYCBO	·	sp:RL2_MYCLE	sp.RS19_MYCTU	
		ORF (bp)	365	465	2115	2160	144	228	153	729	792	1035	1035	516	303	654	687	654	303	327	840	276	285
45		Termina: (nt)	523059	523533	526010	523911	526013	526894	527607	528768	528779	529592	530748	532523	533401	534090	533401	534743	535048	534746	535915	536210	535899
50		Initial (r.t)	522694	523369	523896	525070	526156	527121	527759	528040	529570	530628	531782	532008	533099	533437	534087	534090	534746	535072	535075	535935	536183
		SEQ NO (a.a.)	4053	4054	4055	4056	4057	4058	4059	4060	4961	4962	4063	4364	4065	4066	4067	4068	4069	4070	4071	4072	4073
55		SEO NO:	553	554	555	_	557	558	559	560	561	562	563	564	585	566	567	568	569	570	573	572	573

			, <b></b>						_															
5		Function	50S ribosomal protein L22	30S ribosomal protein S3	50S ribosomal protein L16	50S ribosomal protein L29	30S ribosomal protein S17				50S ribosomal protein L14	50S ribosomal protein L24	50S ribosomal protein L5		2,5-diketo-D-gluconic acid reductase		formate dehydrogenase chain D	molybdopterin-guanine dinucleotide biosynthesis protein	formale dehydrogenase H or alpha chain			ABC transporter ATP-binding protein		
15		Matched length (a.a.)	109	239	137	29	82				122	105	183		260		298	94	756			524		
20		Similarity (%)	91.7	91.2	88.3	1.88	89.0				95.1	91.4	92.3		74.2		59.7	68.1	53.4			52.6		
		Identity (%)	74.3	77.4	69.3	65.7	69.5				83.6	75.2	73.6		52.3		28.9	37.2	24.3	 		26.9		
	Table 1 (continued)	ous gene	uberculosis blV	ovis BCG rpsC	ovis BCG rpIP	ovis BCG rpmC	ovis BCG rpsQ				iberculosis SIN	rberculosis	s rplE		Sp.		genes fdhD	Picolor A3(2)	軐			iberculosis appD		
35	Table 1	Homologous gene	Mycobacterium tuberculosis H37Rv Rv0708 rplV	Mycobacterium bovis BCG rpsC	Mycobacterium bovis BCG rpiP	Mycobacterium bovis BCG rpmC	Mycobacterium bovis BCG rpsQ				Mycobacterium tuberculosis H37Rv Rv3714 rplN	Mycobacterium tuberculosis H37Rv Rv0715 rp!X	Micrococcus luteus rplE		Corynebacterium sp.		Wolinella succinogenes fdhD	Streptomyces coelicolor A3(2) SCGD3.29c	Escherichia coli fdF			Mycobacterlum tuberculosis H37Rv Rv1281c oppD		
40	,	db Match	Sp. RL22_MYCTU	sp:3S3_MYCBO	Sp:RL16_MYCBO	Sp: 3L29_MYCBO	sp:3817_MYCBO				sp:RL:14_MYCTU	sp.RL24_MYCTU	sp:RLS_MICLU		sp.2DKG_CORSP (		sp:FDHD_WOLSU	gp: SCGD3_29	Sp.FDHF_ECOU			sp:YC81_MYCTU		
		ORF (bp)	363	744	414	228	276	294	313	969	366	312	573	1032	807	492	915	336	2133	756	804	1662	1146	1074
45		Terminal (nt)	536576	537322	537741	537971	538252	537974	538381	538718	540106	540423	540998	542079	542090	542921	543415	544335	544757	548084	549187	548990	550699	551854
50		Initial (nt)	5362:7	536579		537724	537977	538267	538698	539413	539741	540112	540426	541048	542856	543412	544329	544670	546889	547329	548990	550651	551844	4095 552927
		SEO NO Se 8	4074	4075	4076	: 4077	4078	4079	4080	4081	4082	4083	4084	4085	4086	4087	4088	4089	4090	4091	4092	4093	4094	4095
<b>55</b>	.	SEQ (DNA)	574	575	576	577	578	579	580	581	582	583	584	585	586	587	588	585	290	59.	592	593	594	595

			_		_												$\overline{}$		7	$\neg \neg$				
5		Function	ein	ein	otein S8	otein L6	otein L18	rolein S5	rotein L30	rotein L15		methylmalonic acid semialdehyde dehydrogenase		onent regulatory	aldehyde dehydrogenase or betaine aldehyde dehydrogenase				-	dehydrogenase	tein	phosphoeno!pyruvate synthetase	phosphoenolpyruvate synthetase	00
10		Ful	hypothetical protein	hypothetical protein	30S ribosomal protein S8	50S ribosomal protein L6	50S ribosomal protein L18	30S ribosomal prolein S5	50S ribosomal protein L30	50S ribosomal protein L15		methylmalonic ad dehydrogenase		novel two-component regulatory system	aldehyde dehydrogenase aldehyde dehydrogenase			reductase	2Fe2S ferredoxin	p-cumic alcohol dehydrogenase	hypothetical protein	phosphoeno!pyr	phosphoenolpyr	cytochrome P450
15		Matched length (a a)	405	150	132	179	110	171	55	143		128		125	487			409	107	257	20	629	378	422
20		Similarity (%)	50.4	66.7	97.7	87.7	6.06	88.3	76.4	87.4		68.8		52.0	71.5			71.6	66.4	70.8	26.0	45.0	66 7	65.2
		Identity (%)	24.7	42.7	75.8	59.2	67.3	67.8	54.6	66.4		46.9		47.0	41.7			41.1	47.7	35.8	50.0	22.9	386	34.8
25	ntinued)	gene	dus AF1398	urans			rpIR	rpsE	2 rpmJ	Og		solor msdA		nse carR	ochrous			recA2	latus fdxE	da cymB	(1 APE0029	s Vc1 DSM	s Vc1 DSM	ropolis thcB
30	Table 1 (continued)	Homologous gene	Archaeoglobus fulgidus AF1398	Deinococcus radiodurans DR0763	Micrococcus luteus	Micrococcus luteus	Micrococcus luteus rpIR	Micrococcus luteus rpsE	Escherichia coli K12 rpmJ	Micrococcus luteus rp10		Streptomyces coelicolor msdA		Azospirillum brasilense carR	Rhodococcus rhodochrous plasmid pRTL1 orf5			Sphingomonas sp. recA2	Rhodobacter capsulatus fdxE	Pseudomonas putida cymB	Aeropyrum pernix K1 APE0029	Pyrococcus furiosus Vc1 DSM 3638 ppsA	Pyrococcus furiosus Vc1 DSM 3638 ppsA	Rhodccoccus enythropolis thcB
35 40		db Match	pir.E69424	gp:AE001531_13	pir. S29885	pir S29886	sp:RL18_MICLU	sp:RS5_MICLU	sp:RL30_ECOLI	Sp:RL15_MICLU		prf:2204281A		GP.ABCARRA_2	prf.2516399E			prf.2411257B	prf.2313249B	gp:PPU24215_2	PIR:H72754	pir.JC4175	pir.JC4176	1290 prt.2104333G
		ORF (bp)	1182	468	396	534	402	633	183	444	729	321	363	456	1491	735	306	1266	318	744	213	1740	1080	
45		Te:minal (nt)	552948	554452	555726	556282	556690	557366	55755	558008	556860	558197	558607	560260	559144	560634	562937	561368	562646	562993	564083	563732	565680	566799
5 <i>0</i>		Initial (nt)	554129	554919	555331	555749	556289	556734		557565	557588		558969	<del></del>	560634	561368	562632	562633	562963			.1	566759	568088
		SEO NO	4096	4097	4098	4099	4100	410	4102	4103	4104	4105	4106	4107	4108	4109	4110	4111	4112	4113	1	4115	4116	4117
	سر.	SEO.	596	597	598	599	909	109	209	603	604	:	909	607	809	609	6:0	611	612	613	614	615	9,9	6:7

								_	-						$\neg$		
5			lion	SSOF			eptidase		factor IF-1	ein S13	ein S11	ein S4	Ipha subunit	-	ein L17	nthase A	rane protein
10			Function	transcriptional repressor	adenylate kinase		methionine aminopeptidase		translation initiation factor IF-1	30S ribosomal protein S13	30S ribosomal protein S11	30S ribosomal protein S4	RNA polymerase alpha subunit		50S ribosomal protein L17	pseudouridylate synthase A	hypothetical membrane protein
15			Matched length (a.a.)	256	184		253		72	122	134	132	311		122	265	786
20			Similarity (%)	66.0	81.0		74.7		86.0	91.0	93.3	93.9	77.8		77.1	61.1	51.2
			Identity (%)	28.5	48.9		43.1		0.77	66.4	61.3	82.6	51 1		51.6	37.0	24.8
25		rtinued)	gene	arotovora	adk		map			lus HB8	:olor A3(2)	erculosis ISD	гроА		2 rpIQ	2 truA	erculosis
<i>30</i>		Table 1 (cortinued)	Homologous gene	Erwinia carotovora carotovora kdgR	Micrococcus luteus adk		Bacillus subtilis 168 map		Bacillus subtilis infA	Thermus thermophilus HBB rps13	Streptomyces coelicolor A3(2) SC8G4.36 rpsK	Mycobacterium tuberculosis H37Rv RV3458C rpsD	Bacillus subtilis 168 rpoA		Escherichia coli K12 rplQ	Escherichia coli K12 truA	Mycobacterium tuberculosis
40	·		db Malch	prf.2512309A	sp:KAD_MICLU		SP. AMPM_BACSU		pir.F69644	pr':2505353B	sp.RS11_STRCO	prt.2211287F	Sp. RPOA_BACSU		sp.RL17_ECOLI	sp:TRUA_ECOLI	2397 pir.G70695
			ORF (bp)	804	543	612	792	828	216	365	402	603	1014	156	489	967	2397
45			Terminal (nt)	568272	571316	570756	572267	573176	573622	574181	574588	575217	576351	575211	576998	577923	580429
50			Initial (nt)	569075	570774	571367	571476	572349	573407	573816	574187	574615	575338	575366	576410	577057	578033
			SEO NO.	4118	4119	4120	4121	4122	4123	4124	4125	4126	,4127	4128	629   4129	630 4130	4131
55			SEQ NO.	618	619	620	62,	622	623	624	625	929	627	628	629	630	631

cyclopropane-fatty-acyl-phospholipid synthase hypothetical membrane protein cell elongation protein hypothetical protein 7 505 485 423 100 50.9 56.0 59.0 53.8 28.0 22.B 30.7 27.4 Streptomyces coelicolar A3(2) SCL2.30c Arabidoosis thaliana CV DIM Mycobacterium tuberculosis H37Rv Rv3283 Escherichia coli K12 cfa H37Rv Rv3779 1545 Sp.DIM\_ARATH sp:CFA\_ECO:J gp:SCL2\_30 pir.A70836 580429 | 2397 | pir.G70695 1353 1257 , 426 456 363 584228 585520 586248 580919 582562 580436 4131 578033 581406 564268 565823 581221 4135 562684 4132 580891 4134 4133 4136 637 : 4137 634 632 635 633 636

5			inase	rotein	protein					arget ESAT-	13	6	ıtase							
10		Function	high-a!kaline serine proteinase	hypothetical membrane protein	hypothetical membrane protein				hypothetical protein	early secretory antigen target ESAT- 6 protein	50S ribosomal protein L13	30S ribosomal protein S9	phosphoglucosamine mutase		hypothetical protein			hypothetical protein	alanine racemase	hypothelical protein
15		Matched length (a.a.)	273	516	1260				103	80	145	181	450		318			259	368	154
20		Similarity (%)	58.0	50.6	38.4	!			6.69	81.3	82.1	72.4	76.4		45.6			72.2	68.5	78.6
		Identity (%)	31.3	24.0	65.0				31.1	36.3	58.6	49.2	48.9		29.3			44.0	41.6	48.7
25 30	Table 1 (continued)	Homologous gene	Bacillus alcalophilus	Streptomyces coelicolor A3(2) SC3C3.21	Mycobacterium tuberculosis H37Rv Rv3447c				Mycobacterium tuberculosis H37Rv Rv3445c	Mycobacterium tuberculosis	Streptomyces coelicolor A3(2) SC6G4.12. rpIM	Streptomyces coelicolor A3(2) SC6G4, 13. rpsl	Staphylococcus aureus femR315		Synechocystis sp. PCC6803 slr1753			Mycobacterium leprae B229_F1_20	Myccbacterium tuberculosis H37Rv RV3423C alr	Myccbaderium tuberculosis H37Rv Rv3422c
35	Ţe	£	Bacillus a	Streptomy SC3C3.21	Mycobact H37Rv Rv				Mycobact H37Rv Ry	Mycobact	Streptomy SC6G4.17	Streptomyces co SC6G4.13. rpsl	Staphyloc femR315		Synechoo s!r1753			Mycobacteriu B229_F1_20	Myccbact H37Rv R	Myccbad H37Rv R
40		db Match	sp.ELYA_BACAO	pir.T10930	pir:E70977				pir.C70977	prf:2111376A	sp:RL13_STRCO	sp:RS9_STRCO	prf:2320260A	;	pir:S75138	,		pir:S73000	Sp.ALR_MYCTU	sp:Y097_MYCTU
		ORF (bp)	1359	1371	3567	822	663	906	324	288	441	546	1341	303	1509	573	234	855	1083	495
45		Terminal (nt)	586399	587645	592862	589590	589898	593761	594258	594580	595379	595927	597449	598194	599702	598778	599932	600022	602053	602574
50		Initial (nt)	587757	589015	589296	590411	590560	592862	593935	594293	594939	595382	596109	597892	598194	599350	599699	600876	600971	602080
		SEQ NO.	4138	4139	4140	4141	4142	4143	4144	4145	4146	4147	4148	4149	4150	4151	4152	4153	4154	4155
55		SEQ NO (DNA)	638	639	640	641	642	643	644	645	646	647	648	649	650	651	652	653	654	655

5	Function	550 hypothetical membrane protein	
15	Matched length (a.a.)	550	
20	Identity Similarity Matched (%) (%) (a.a.)	66.2	
	Identity (%)	28.9	
25 (panuj	eue	idE	
S Table 1 (continued)	Homologous gene	Escherichia coli K12 yidE	
35			
40	db Match	1599 sp.YIDE_ECOLI	
	ORF (bp)		
45	Terminal ORF (nt)	604409	
50	Initial (nt)	4156 602811	
	SEQ NC (e.e.)	4156	
	0 - 3	10	ĺ

Function	hypothetical membrane protein	proline iminopeptidase	hypothetical protein	ribosomal-protein-alanine N- acetyltransferase	O-sialoglycoprotein endopeptidase	hypothetical protein			heat shock protein groES	heat shock protein groEL	hypothetical protein	hypothetical protein	regulatory protein	RNA polymerase sigma factor		hypothetical protein	IMP dehydrogenase	hypothetical protein
Matched length (a.a.)	550	411	207	132	319	571			100	537	75	138	94	174		1:6	504	146
Similarity (%)	66.2	9'22	75.4	59.9	75.2	59.4			94.0	85.1	56.0	45.0	88.3	81.6		69.8	93.9	53.0
Identity (%)	28.9	51.3	52.2	30.3	46.1	38.4			76.0	63.3	50.0	34.0	64.9	55.2		41.4	80.8	39.0
Homologous gene	Escherichia coli K12 yidE	Propionibacterium shermanii pip	Mycobacterium tuberculosis H37Rv Rv3421c	Escherichia coli K12 riml	Pasteurella haemolytica SERCTYPE A1 gcp	Mycobacterium tuberculosis H37Rv Rv3433c			Mycobacterium tuberculosis H37Rv RV3418C mopB	Mycobacterium leprae B229_C3_248 groE1	Mycobacterium tuberculosis	GP:MSGTCWPA_3 Mycobacterium tuberculosis	Mycobacterium smegmatis whiB3	Mycobacterium tuberculosis H37Rv Rv3414c sigD		Mycobacterium leprae B1620_F3_131	Corynebacterium ammoniagenes ATCC 6872 guaB	Pyrocaccus horikashii PH0308
db Match	sp:YIDE_ECOLI	gp:PSJ00161_1	sp:Y098_MYCTU	sp:RIMI_ECOLI	sp:GCP_PASHA	sp:Y115_MYCTU			sp:CH10_MYCTU	sp.CH61_MYCLE	GP:MSGTCWPA_1	GP:MSGTCWPA_3	gp:AF073302_1	sp Y09F_MYCTU		Sp YO3H_MYCLE	gp:AB003154_1	PIR:F71458
ORF (bp)	1599	1239	675	507	1032	1722	429	453	297	1614	255	1158	297	564	1026	378	1518	627
Terminal (nt)	604409	605708	606392	606898	607936	609679	610175	609816	610544	612272	610946	611109	612418	613719	614747	614903	616853	615605
Initial (nt)	602811	604470	605718	606392	606905	607958	609747	610268	610348	610659	611200	612266	612714	613156	613722	615180	615336	616231
SEQ NO.	4156	4157	4158	4159	4160	4161	4162	4163	4164	4165	4166	4167	4168	4169	4170	4171	4172	4173
SEQ NO.	i —	657	658	629	099	661	299	693	664	665	999	299	899	699	029	671	672	673

EP 1 108 790 A2

																					$\overline{}$
5		Function	IMP dehydrogenase	hypothetical membrane protein	glutamate synthetase positive regulator	GMP synthetase	٠			hypothetical membrane protein	two-component system sensor histidine kinase	transcriptional regulator or extracellular proteinase response regulator				hypothetical protein	hypothetical protein		hypothetical protein	hypothetical membrane protein	
15		Matched length (a.a.)	381 IN	274 h	252 g	517 G				513 h	411	218 e	_	-		201 h	563 h		275 h	288 h	
20		Similarity (%)	86.1	67.5	58.4	92.8				39.6	48.7	65.1				64.2	64.1		67.9	58.3	
		Identity (%)	70.9	38.0	29.0	81.6				20.5	26.8	33.5				30.9	37.5		33.8	27.8	
25	Table 1 (continued)	us gene	TCC 6872	.12 ybiF	tc	uaA				elicolor A3(2)	slicolor A3(2)	68 degU				berculosis	berculosis		elicoior A3(2)	iodurans	
30	Table 1 (	Homologous gene	Corynebacterium ammoniagenes ATCC 6872	Escherichia coli K12 ybiF	Bacillus subtilis gltC	Corynebacterium ammoniagenes guaA				Streptomyces coelicolor A3(2)	Streptomyces coelicolor A3(2) SC6E10.15c	Bacillus subtilis 168 degU	-			Mycobacterium tuberculosis H37Rv Rv3395c	Mycobacterium tuberculosis H37Rv Rv3394c		Streptomyces coelicolor A3(2) SC5B8 20c	Deinococcus radiodurans DR0809	<u> </u>
35		db Match	gp:AB003154_2 a	sp:YBIF_ECOLI E	prf 1516239A B	Sp.GUAA_CORAM				gp.SCD63_22 S	25	sp.DEGU_BACSU B							gp:SC588_20	gp.AE001935_7	
40				<del>i                                    </del>					6			<del> </del>	-	6	3	5 pir B70975	10 pir.A70975	0			0
		OR (dg)	1122	921	606	1569	663	44	189	1176	1140	069	324	489	963	825	159(	099	861	861	390
45		Terminal (nt)	618094	618093	619994	621572	620264	622157	622457	622460	624939	525674	926000	626370	626577	528551	630140	63015	531809	631824	632590
50		Initial (nt)	616973	619013	619086	620004	620926	621717	62229	623635	623800	624985	625677	625558	627539	627727	628551	630810	633949	632684	633079
		SEQ NO.	4174	4175	4176	4177	4178	4179	4180	4181	4102	4183	4184	4185	4186	4187	4188	4189	419C	4191	4192
55		SEQ NO.	674	675	676	677	678	579	980	681		683	684	585	989	587	588	689	069	591	692

			·																		
5		uo	ine protein			sport protein	ohosphate	itor (MarR	protein											-	
10		Function	hypothetical membrane protein	phytoene desaturase	phytoene synthase	transmembrane transport protein	geranylgeranyl pyrophosphate (GGPP) synthase	transcriptional regulator (MarR family)	outer membrane lipoprotein	hypothetical protein	DNA photoiyase	glycosyl transferase	ABC transporter	ABC transporter		ABC transporter		ABC transporter	lipopratein	DNA polymerase III	hypothetical protein
15		Matched length (a.a.)	95	524	288	722	367	188	145	462	497	205	897	223		206		346	268	1101	159
20		Similarity (%)	67.4	76.2	71.2	75.6	63.8	68.1	62.1	74.2	63.2	53.7	54.9	72.2		75.2		75.4	67.2	57.5	62.3
		Identity (%)	36.8	50.4	42.0	48.6	32.7	38.3	33.1	48.7	40.0	25.9	24.3	35.4		35.9		43.6	28.7	30.2	41.5
25	(penu	92	F	VTCC	\TCC	r A3(2)	뷛		OS60 blc		TCC	¥	r A3(2)	0		0		apc	<b>a</b>	ını	r A3(2)
30	Table 1 (continued)	Homologous gene	Mycobacterium mar.num	Brevibacterium linens ATCC 9175 crtl	Brevibacterium linens ATCC 9175 crtB	Streptomyces coelicolor A3(2) SCF43A.29c	Brevibacterium linens crtE	Brevibacterium linens	Citrobacter freundii olc OS60 blc	Brevibacterium linens	Brevibacterium linens ATCC 9175 cpd1	Streptococcus suis cps1K	Streptomyces coelicolor A3(2) SCE25.30	Bacillus subtilis 168 yvrO		Helicobacter pylori abcD		Escherichia coli TAP90 abc	Haemophilus influenzae SEROTYPE B hipA	Thermus aquaticus dnaE	Streptomyces coelicolor A3(2) SCE126.11
<i>35</i>		cb Match	gp:MMU92075_3	gp:AF139916_3	gp:AF139916_2	gp:SCF43A_29	gp:AF139916_11	gp:AF139916_14	Sp.BLC_CITFR (	gp.AF139916_1	2.	gp AF155804_7	gp SCE25_30	prf.2420410P		prf:2320284D		sp. ABC_ECOLI	SP.HLPA_HAEIN	prf.2517386A	gp:SCE126_11
		(dq) 380	396	1644	912	2190	1146	585	648	1425	1404	753	2415	717	153	999	846	1090	268	3012	447
45		Terminal (nt)	633079	633532	635178	636089	638317	640208	640232	642557	642556	844778	545176	647593	648315	648440	650187	649114	650392	654612	655122
50		Iritia (n1)	633474	635-75	636089	638278	639462	639624	640879	641133	643959	644026	647590	648309	648467	649105	649342	650193	651288	651601	654676
		SEQ NO. (a a)	4193	4194	4195	4196	4197	4198	4199	1200	4201	4202	4203	4204	4205	4206	4207	4208	4209	42:0	42.1
55		SEQ NO DNA)	593	594	969	969	269	969	669	700	701	702	703	704	705	902	707	708	602	710	711

EP 1 108 790 A2.

		<del></del>	$\overline{}$				- 1	$$ $\top$										-	- 1	- 1
5	Function	hypothetical membrane protein	-	transcriptional repressor	hypothetical protein		transcriptional regulator (Sir2 family)	hypothetical protein	iron-regulated lipoprote:n precursor	rRNA methylase	methylenetetrahydrofolate dehydrogenase	hypothetical membrane protein	hypothetical protein		homoserine O-acetyltransferase	O-acetylhomoserine sulfhydrylase	carbon starvation protein		hypothetical protein	
15	Matched length (a.a.)	468 hy		203 tr	264 h		245 tr	157 h	357 ir	151 rF	278 d	و 9	489 h		379 h	429	069		20	
20	Similarity (%)	56.0		76.4	61.7		71.8	78.3	62.2	86.1	87.4	76.3	63.2		99.5	76.2	78.4		0.99	
	Identity (%)	26.1		50.3	34.9		42.5	45.2	31.1	62.9	70.9	31.3	34.0		99.5	49.7	53.9		40.0	
25 (panujuo	s gene	icolor A3(2)		perculosis R	icolor A3(2)		gidus AF1676	icolor A3(2)	diphtheriae	berculosis oU	berculosis olD	ргае	licolor A3(2)		glutamicum	metY	12 cstA		12 yjiX	
& Table 1 (continued)	Homologous gene	Streptomyces coelicolor A3(2) SCE9 01		Mycobacterium tuberculosis H37Rv Rv2788 sirR	Streptomyces coelicolor A3(2) SCG8A.05c		Archaeoglobus fulgidus AF 1676	Streptomyces coe'icolor A3(2) SC5H1.34	Corynebacterium diphtheriae irp1	Mycobacterium tuberculosis H37Rv Rv3366 spoU	Mycobacterium tuberculosis H37Rv Rv3356c folD	Mycobacterium leprae MLCB1779.16c	Streptomyces coelicolor A3(2) SC66T3.18c		Corynebacterium glutamicum metA	Leptospira meyeri met <sup>y</sup>	Escherichia coli K12 cstA		Escherichia coli K12 yjiX	
35		35		¥ ¥	18 S		¥	8 8	S ë	ΣÏ	ΣÏ		ळ ळ		υE	د		-	ш	$\dashv$
40	db Match	gp:SCE9_1		pir.C70884	gp:SCG8A_5		pir.C69459	gp:SC5H1_34	gp:CDU02617_1	pir.E70971	pir.C70970	gp:MLCB1779_8	gp.SC6673_18		gp:AF052652_1	pri 2317335A	SP.CSTA_ECOLI		sp:YJX_ECOL!	
	ORF (bp)	1413	738	699	798	138	774	492	966	471	852	255	1380	963	1131	1311	2202	609	201	609
45	Terminal (nt)	656534	655397	657215	657205	658142	658928	659424	660538	660650	662017	662374	562382	564126	565183	666460	670465	669445	670672	671045
50	Initial (nt)	655122	655834	656547	658002	658005	658155	658933	659543	661120	661.66	662120	663761	665088	666313	667770	668264	670053	670472	671653
	SEQ NO.	4212	4213	4214	4215	4216	4217	4218	4215	4220	4221	4222	4223	4224	4225	4226	4227	4228	4229	4230
55	SEQ NO (DNA)		713	714	715	716	717	718	719	720	721	722	723	724	725	726	721	728	1 .	730
		4	1	1	1		•	·			<b></b>									

			т —	<del>'</del>	<del>,</del>	_	<del></del>		-r	., .		<del>_,</del>								
5		c.		pyruvate					15.6			protein	binding protein			ein precursor	ance profein	ontrol protein		
10		Function	hypothetical protein	carboxy phosphoenolpyruvate mutase	citrate synthase		hynothetical protein	man di mananadi.	L-malate dehydrogenase	regulatory protein		vibriobactin utilization protein	ABC transporter ATP-binding protein	ABC transporter	ABC transporter	iron-regulated lipoprotein precursor	chloramphenicol resistance protein	catabolite repression control protein	hypothetical protein	
15		Matched length (aa)	317	281	380		53	3	338	226		284	269	339	330	356	395	1	<del>                                     </del>	
20		Similarity (%)	86.4	76.2	81.3		623		67.5	62.8		54.2	85.1	86.4	88.2	82.3	69.6	58.1	85.8	
		Identity (%)	71.0	41.6	56.1		34.0		37.6	26.1		25.4	55.4	56.3	63.0	53.	32.2	30.4	56.2	
25	ontinued)	gene	erculosis	scopicus	gmatis		vneC		Methanothermus fervidus V24S mdh	Bacillus stearothermophilus T-6 uxuR		WA 395	htheriae	htheriae	htheriae	htheriae	refae cmlv	inosa crc	ae Rd	
30	Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv1130	Streptomyces hygroscopicus	Mycobacterium smegmatis ATCC 607 gltA		Escherichia coli K12 yneC		thermus fer	stearothern		Vibrio cholerae OGAWA 395 viuB	Corynebacterium diphtheriae	Corynebacterium diphtheriae	Corynebacterium diphtheriae irp18	Corynebacterium diphtheriae	Streptomyces venezuelae cmlv	Pseudomonas aeruginosa crc	Haemophilus influenzae Rd H:1240	
35		<b>-</b>	Mycobac H37Rv F	Strepton	Mycobacterium ATCC 607 gltA		Escheric		Methano mdh	Bacillus s uxuR		Vibrio ch	Coryneba irp 1D	Coryneba irp1C	Coryneba irp1B	Coryneba irp1	Streptomy	Pseudom	Haemoph H:1240	
40		db Match	pir C73539	prf. 1902224A	sp:CISY_MYCSM		SP.YNEC_ECOL!		SP.MOH_METFE	pri:25:4353L		sp:V:UB_VIBCH	gp.AF176902_3	gp.AF176902_2	gp:AF*76902_1	gp:CD!J02617_1	prf:22C2262A	prf:22222208	sp:YICS_HAEIN	
		ORF (tp)	954	912	1149	930	192	672		720	702	897	907	1059	966	1050	1272	912	657	195
45		Terminal (nt)	672653	673576	674756	672710	674799	675846	675082	676218	677047	680131	681040	681846	682871	683876	686380	687346	688007	688335
50		Initiat (nt)	671700	672665	673608	673639	674990	675175	676122	676937	677748	691027	681846	682904	683866	684925	685109	586435	687351	4245 588141
	-	(a.a.)	4231	4232	4233	4234	4235	42.36	4237	4238	4239	4240	4241	4242	4243	4244	4245	4245	4247	4248
55	0	NO (AND)	731	732	733	734	735	736	737	738	739	740	741	742	743		745	746	747	748

EP 1 108 790 A2

	Function		feriichrome ABC transporter	hemin permease	tryptophanyl-tRNA synthetase	hypothetical protein		penicillin-binding protein ob precursor	hypothetical protein	hypothetical protein			uracil phosphoribosyltransferase	bacterial regulatory protein, laci family	N-acy-L-amino acid amidohydrolase or peptidase	phosphomannomutase	dihydrolipoamide dehydrogenase	pyruvate carboxylase	hypothetical protein	hypothetical protein
	Matched length (aa)		244	346	331	278		301	417	323			209	77	385	561	468	1140	263	127
	Similarity (%)		73.8	69.1	79.8	72.3		57.5	70.7	52.6			72.3	66 2	80.5	53.8	65.0	100.0	60.1	699
	Identity (%)		45.1	38.7	54.4	37.1		30.9	34.1	29.4			46.4	41.6	51.4	22.1	31.6	100.0	26.2	30.7
Table 1 (continued)	Homologous gene		Corynebacterium diphtheriae hmuV	Yersinia enterocolitica hemU	Escherichia coli K12 trpS	Escherichia co'i K12 yhjD		Salmonella typhimurium LT2 dacD	Mycobacterium tuberculosis H37Rv Rv3311	Streptomyces coelicolor A3(2) SC6G10.08c			Lactococcus lactis upp	Streptomyces coelicolo: A3(2) SC1A2.11	Mycobacterium tuberculosis H37Rv Rv3305c amiA	Mycoplasma pirum JER manB	Halobacterium volcanii ATCC 29605 lpd	Corynebacterium glutamicum strain21253 pyc	Mycobacterium tuberculosis H37Rv Rv1324	Streptomyces coelicolor A3(2) SCF11.30
	db Match		gp:AF109162_3	pir.S54438	Sp.SYW_ECOLI			sp:DACD_SALTY	pir.F73842	gp:SC6G10_8			Sp.UFP_LACLA	gp:SC1A2_11	pir H70841	SP. MANB_MYCPI	Sp:DLDH_HALVO	prf.2415454A	sp YD24_MYCTU	gp:SCF11_30
	ORF (bp)	975	780	1017	1035	1083	903	1137	1227	828	195	351	633	384	1182	1725	1407	3420	870	486
	Terminal (nt)	6389:6	689917	90/069	692916	694110	695074	695077	696769	698065	699266	698922	699913	700381	703262	700384	704811	708630	709708	710278
	Initia! (nt)	68989	969069	691722	691882	693028	694172	696213	697995	698922	699072	!		866669	702081	702108	703405	705211	708839	709793
	SEQ NO.	4249	4250	4251	4252	4253	4254	4255	4256	4257	4258	4259	4260	4261	4262	4263	4264	4265	4266	4257
	SEO NO (DNA)		1	751	1.	1	754	<del>                                     </del>	756	757	+	759	760	76:	762	763	764	765	766	767

			_						1			7				<del>,                                     </del>	<del></del>				
5					nate	yruvate							erase			e protein			scuer or	scuer or	
10		Function	hypothetical protein	thioredoxin reductase	PrpD protein for propionate catabolism	carboxy phosphoenolpyruvate mutase	hypothetical protein	citrate synthase		hypothetical protein			thiosulfate sulfurtransferase	hypothetical protein	hypothetical protein	hypothetical membrane protein	hypothetical protein	hypothetical protein	detergent sensitivity rescuer or carboxyl transferase	defergent sensitivity rescuer or carboxyl transferase	
15		Matched length (a.a.)	381	305	521	278	96	383		456			225	352	133	718	192	63	537	543	
20		Similarity (%)	69.0	59.3	49.5	74.5	47.0	78.9		72.6			100.0	79.8	76.7	63.4	66.2	69.8	100.0	100.0	
		Identity (%)	44.6	24.6	240	42.5	39.0	546		408			100.0	61.1	51.1	35.1	31.8	33.3	8.66	93.6	
25	Table 1 (continued)	ens gene	68 yciC	359 trxB	nurium LT2	groscopicus	K1 APE0223	negmatis		berculosis			glutamicum	juni Cj0069	prae	berculosis	12 yceF	prae 81308-	gluta:micum	glutamicum	
30	Table 1	Homologous gene	Bacillus subtilis 168 yciC	Bacillus subtilis IS59 txB	Salmonella typhimurium LT2 prpD	Streptomyces hygroscopicus	Aerapyrum pernix K1 APE0223	Mycobacterium smegmatis ATCC 607 gltA		Mycobacterium tuberculosis H37Rv Rv1129c		 	Corynebacterium ATCC 13032 thtR	Campylobacter jejuni Cj0069	Mycobacterium leprae MLCB4.27c	Mycobacterium tuberculosis H37Rv Rv1565c	Escherichia coli K12 yceF	Mycobacterium leprae 81308- C3-211	Corynebacterium AJ11060 dtsR2	Corynebacterium AJ11060 dtsR1	
<i>35</i> .		fg.		BACSU						2 1						≥ I				04	
40		db Match	6 pir.869760	sp:TRXB_B	Sp.PRPD_SALTY	prf. 1502224A	PIR.E72779	2 sp.CISY_MYCSM		3 pir.B70539			sp:THTR_CORGL	gp:C_11168X1_62	gp:MLCB4_16	pir.G70539	sp:YCEF_ECOLI	prf.2323363CF	gp:AB018531_2	pir.JC4991	
		ORF (bp)	1086	924	1494	888	378	1182	375	1323	246	1359	903	1065	414	2148	591	246	1611	1629	
45	į	Terminal (nt)	710520	712647	714231	715145	714380	716283	716286	716687	718350	720016	720547	722841	722925	725559	725872	726470	726742	728696	
50		Initial (nt)	711635	7-1724	712738	714258	714757	7:5102	7.6630	718009	7:8105	7:8658	721449	721777	723338	723412	726452	726715	728352	730324	
		SEQ NO	4268	4259	4270	4271	4272	4273	4274	4275	4276	4277	4278	4279	4280	4281	4282	4283	4284	4285	
55	] :: سـ ِ	SEO NO. (DNA)	768	769	770	771	772	773	77.4	775	776	777	778	779	780	781	782	783	784	785	
																			<del></del>		

EP 1 108 790 A2

Table 1 Continued    Table 1																			. —	
SEC   Initial   Terminal   ORF   Ctb Match   Homologous gene   (%)   (			Function	bifunctional protein (biotin synthesis repressor and biotin acetyl-CoA carboxylase ligase)	hypothetical membrane protein	5'-phosphoribosyl-5-amino-4- imidasol carboxylase	K+-uptake protein			5'-phosphoribosyl-5-amiro-4- imidasol carboxylase	hypothetical protein	hypothetical protein	nitrilotriacetate monooxygenase	transposase (ISA0963-5)	glucose 1-dehydrogenase	hypothetical membrane protein		hypothetical protein	hypothetical protein	
SEQ   Initial   Terminal   ORF   Cb Match   Homologous gene   (%)	15		Matched length (a.a.)	293	165	394	628			147	152	255	426	303	256	96		175	14.2	
Secondary   Seco	20	ļ	Similarity (%)	61.8	58.8	83.8	73.6			93.2	60.5	70.6	73.0	52.5	64.8	8.89		66.3	76.8	
SEQ Initial Terminal ORF Cb Match (a.a.) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt			Identity (%)	28.7	23.0	69.0	41.1			85.7	36.2	42.8	. 43.2	23.4	31.3	29.2		28.6	35.9	
SEQ Initial Terminal ORF Cb Match (a.a.) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt	25	continued)	ns gene	12 birA	berculosis	TCC 6872	.12 kup			TCC 6872	reliosum	elicolor A3(2)	intzii ATCC	ılgidus	um IAM 1030	tima MSB8		68 ywjB	elicolor A3(2)	
SEQ Initial Terminal ORF Cb Match (a.a.) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (nt) (bp) Cb Match (a.a.) (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt	30	Table 1 (	Hamologo	scherichia coli K	hycobacterium tu	corynebacterium mmoniagenes A	scherichia coll K			Corynebacterium immoniagenes A vur£	Actinosynnema p	Streptomyces cou SCF43A.36	Chelatobacter he 29600 ntaA	Archaeoglobus fu	Bacillus megateri gdhil	Thermotoga mari TM1408		Bacillus subtills 1	Streptomyces co SCJ9A.21	
SEO Intial Terminal ORF (n1) (n1) (n1) (n2) (n2) (n3) (n1) (n1) (n2) (n3) (n3) (n3) (n3) (n3) (n3) (n3) (n3			cb Match				ECOLI								-					
SEG Initial Terminal (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt)			JRF (bp)	<del>-i</del>	+	ļ		615	357	<del></del>	1		···· —	<del></del>			342		<del></del>	222
SEQ NO. (a.a.) 4286 4288 4289 4290 4292 4293 4297 4299 4299 4299 4299 4299 4299 4299	45		<u> </u>	<del> </del>	·}	<b></b>	<del>                                     </del>			735896	736351	737204			740228	741765	742195	741818	742828	742831
	5 <i>0</i>		Initial (nt)	730436	731312	731857	733072	733797	734984	·	735899	736413	738529		741016	L		ــــ		743052
25			SEQ NO.	4286	4287	4288	4289	4290	4291	4292	4293	4294	4295	4296	4297	4298	4299	ī	4301	
	55		SEQ NO (DNA)	786	787	788	789	790	.52.	792	793	794	795	796	797	798	799	800	80.	802

5			Function	trehalose/mattose-binding protein	trehalose/maltose-binding protein		trehalose/maltose-binding protein		ABC transporter ATP-binding protein (ABC-type sugar transport protein) or cellobiose/maltose transport protein		RNA helicase			hypothetical protein	hypothetical protein	DNA helicase II					RNA helicase	hypothetical protein	RNA polymerase associated protein (ATP-dependent helicase)
15			Matched length (a.a.)	271	306		417		332		1783			240	720	701					2033	869	873
20			Similarity (%)	75.3	70.3		62.4		73.9		49.9			59.2	62.5	41.1					45.8	53.2	48.6
			identity (%)	42.4	37.3		30.9		57.2		25.1			31.7	30.0	20.7					22.4	24.4	23.1
30	:	Table 1 (continued)	Hcmologous gene	Thermococcus litoralis malG	Thermococcus litoralis malF		Thermococcus litoralis malE		Streptomyces reticuli msiK		Deinococcus radiodurans R1 DRB0135			Mycobacterium tuberculosis H37Rv Rv3268	Helicobacter pylori J99 jhp0462	Escherichia coli K12 uvrD					Streptomyces caelicolor SCH5 :3	Halobacterium sp. NRC-1 plasmid pNRC100 H1130	Escherichia coli K12 hepA
<i>35 40</i>			db Match	prf 2406355C	prf.2406355B		prf.2406355A		prf.2308356A		pir B75633				pir.C71929	1702		-			pir.T36671	pir.T08313	SP HEPA_ECOLI
			ORF (bp)	834	1032	468	1272	423	966	369	4800	372	3699	633	2433	1563	357	393	396	825	6207	4596	2886
45			Terminal (n:)	743067	743900	745046	745622	748442	747031	748814	748886	757434	753697	757630	758364	760906	762853	763122	762582	767367	763237	769547	774150
50			Initial (nt)	743900	744931	745513	746893	748020	748C26	748446	753685	757063	757395	759262	760796	762468	762497	762730	762977	768191	769443	774142	777035
			SEQ NO (a.a.)	4303	4304	4305	4306	4307	4308	4309	43:0	4311	4312	4313	4344	43.5	4316	4317	4318	4319	4320	4321	4322
55			SEQ NO (DNA)	803	804	805	609	607	808	608	610	811	812	813	814	815	816	817	818	819	820	821	822

					_														
5		tion		NAc- renol, a·3-L- ase	nate				tase		nate isomerase			nsive protein		ocysteine			
10		Function	hypothetical protein	dTDP-Rha:a-D-GlcNAc- diphosphoryl polyprenol, rhamnosyl transferase	mannose-1-phosphate guanylyltransferase	regulatory protein	hypothetical protein	hypothetical protein	phosphomannomutase	hypothetical protein	mannose-6-phosphate isomerase			pheromone-responsive protein		S-adenosyl-L-homocysteine hydrolase			thymidylate kinase
15		Matched length (a.a.)	527	289	353	94	139	136	460	327	420			180		476			209
20		Similarity (%)	71.4	77.9	6.99	81.9	74.8	71.3	66.3	56.3	66.2			57.8		83.0			26.0
		identity (%)	45.5	56.4	29.8	73.4	48.9	51.5	38.0	31.2	36.9			35.6		29.0			25.8
25	itinued)	gene	culosis	matis	visiae	jmatis	culosis	olo: A3(2)	eo M40	culosis	manA			is plasmid		lis WAA38			dus VC-16
30	Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv3267	Mycobacterium smegmatis mc2155 wbbl.	Saccharomyces cerevisiae YDL055C MPG1	Mycobacterium smegmatis whmD	Mycobacterium tuberculosis H37Rv Rv3259	Streptomyces coelicolo: A3(2) SCE34.11c	Salmonella montevideo M40 manB	Mycobacterium tuberculosis H37Rv Rv3256c	Escherichia coli K12 man.A			Enterococcus faecalis plasmid pCF10 prgC		Trichomonas vaginalis WAA38			Archaeoglobus fulgidus VC-16 AFC061
35 40		cb Match	M pir.D70978	gp.AF187550_1 m	Sp.MPG1_YEAST	9p.AF164439_1 W	pir.B70847	9p SCE34_11 S	SP MANB_SALMO ST	pir.B70594	sp:MANA_ECOLI E			prt: 1804279K P		Sp.SAHH_TRIVA 1			sp KTHY_ARCFU
		ORF (bp)	1554	897	1044	408	456	390	1374	1005	1182	150	360	564	351	1422	708	720	609
45	-	Terminal (nt)	777158	779910	78117:	781875	782162	783101	784557	785639	786824	787045	787983	787170	788546	790093	788719	789002	790704
50		lritia' (nt)	778711	779014	783128	781468	782617	782712	783184	784635	785643	785896	787624	787733	788196	788672	789426	789721	790096
	نير.	SEQ NO.	4323	4324	4325	4326	4327	4328	4329	4330	4331	4332	4333	4334	4335	4336	4337	4338	4339
55		SEQ SEQ NO. NO. (DNA) (a.a.)	823	824	825	826	827	828	829	830	831	832	833	834	835	936	837	838	839

	,																
10	Function	two-component system response		two-component system sensor histidine kinase	lipoprotein	hypothetical protein		30S ribosomal protein or chloroplast precursor	preprotein translocase SecA subunit		hypothetical protein	hypothetical protein	5-enolpyruvylshikimate 3-phosphate synthase	hypothetical protein	5-enolpyruvylshikimate 3-phosphate synthase	hypothetical protein	RNA polymerase sigma factor
15	Matched lergth			484	595	213		203	845 p		170	322 h	461 5	180	23 5	380 h	188 R
20	Similarity (%)	90.6		78.9	65.6	72.8		61.6	9.66		78.8	82.9	0.66	63.9	100.0	42.4	87.2
	Identity (%)	73.7		53.1	29.6	38.0		34.5	99.1		47.1	64.6	0.86	38.3	100.0	21.6	61.2
Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv3246c mtrA		Mycobacterium tuberculosis H37Rv Rv3245c mtrB	Mycobacterium tuberculosis H37Rv Rv3244c IpqB	Mycobacterium tuberculosis H37Rv Rv3242c		Spinacia oleracea CV rps22	Brevibacterium flavum (Corynebacterium glutamicum) MJ-233 secA		Mycobacterium tuberculosis H37Rv Rv3231c	Mycobacterium tuberculosis H37Rv Rv3228	Corynebacterium glutamicum ASO19 aroA	Mycobacterium tuberculosis H37Rv Rv3228c	Corynebacterium glutamicum	Mycobacterium tuberculosis H37Rv Rv0336	Mycobacterium tuberculosis sigH
40	cb Match	pri.2214304A		prf:2214304B	pir F70592	pir D70592		sp.RR30_SPIOL	gsp:R74093		pir.A70591	pir.F73590	gp:AF114233_1	pir:D70590	GP-AF114233_1	pir.G70506	prf 2515333D
	ORF (bp)	678	684	1497	1704	588	156	663	2535	672	564	987	1413	480	123	1110	618
45	Terminal (nt)	791409	790738	793008	794714	79530:	795292	796110	798784	799691	800200	800208	801190	803128	802565	903131	805025
50	Initial (nt)	790732	791421	791512	793008	794714	795447	795448	795250	799020	799697	801194	802602	802649	802687	804240	804408
	SEO NO.	434C	4341	4342	4343	4344	4345	4346	4347	4348	4349	4350	4351	4352	4353	4354	4355
5	SEQ NO. (Dr.A)	840	841	842	843	844	945	846	847	848	849	950	951	952	853 /	954	855

EP 1 108 790 A2

	Function	regulatory protein	hypothetical protein	hypothetical protein	DEAD box ATP-dependent RNA helicase		hypothetical protein	hypothetical protein	ATP-dependent DNA helicase		ATP-dependent DNA helicase		potassium channel	hypothetical protein	DNA helicase II		hypothetical protein	
	Matched length (a.a.)	84	129	415	458		291	249	1155		1126		302	230	099		280	
	Similarity (%)	96.4	65.1	62.2	64.0		69.8	62.9	48.9		65.7		64.2	58.3	58.8		49.3	
	tdentity (%)	78.6	33.3	29.6	37.3		46.4	37.0	23.9		41.4		26.2	30.4	32.6		26.8	
Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv3219 whiB1	Mycobacterium tuberculosis H37Rv Rv3217c	Mycobacterium tuberculosis H37Rv Rv3212	Klebsiella pneumoniae CG43 deaD		Mycobacterium tuberculosis H37Rv Rv3207c	Mycobacterium tuberculosis H37Rv Rv3205c	Mycobacterium tuberculosis H37Rv Rv3201c		Mycobacterium tuberculosis H37Rv Rv3201c		Methanococcus jannaschii JAL- 1 MJ0138.1.	Mycobacterium tuberculosis H37Rv Rv3199c	Escherichia coli K12 uvrD		Mycobacterium tuberculosis 1137Rv Rv3196	
	db Match	pir.D70596	pir.B70596	pir.E70595	2 sp.DEAD_KLEPN		pir.H70594	pir.F70594	pir.G70951		9 pir.G70951		S sp:Y13B_METJA	pir.E70951	sp.UVRD_ECOLI		pir:B70951	
	ORF (bb)	258	420	1200	1272	225	846	759	3048	780	3219	1332	1005	714	2034	591	8.6	603
	Terminal (rt)	805535	806737	806740	807946	809510	810394	811153	814217	811386	817422	814210	818523	815236	821287	822669	821290	823391
	Initial (nt)	805792	806318	807939	809217	809286	809549	810405	811170	812165	814204	815541	8-75-9	818523	819254	822079	822105	822789
	SEQ NO.	4356	4357	4358	4359	4360	435	4352	4363	4364	4365	4366	4357	4368	4369	4370	4371	4372
	SEQ NO.	856	857	858	859	098	861	862	863	864	865	998	867	868	698	870	871	872

		r									_										
5		٠							oin				recursor		ymerase	PS1 protein					
10 ,		Function	hypothetical protein	hypothetical protein			hypothetical protein	regulatory protein	ethylene_inducible protein	hypothetical protein	hypothetical protein		alpha-lytic proteinase precursor		DNA-directed DNA polymerase	major secreted protein PS1 protein precursor					monophosphatase
15		Matched length	474	350			1023	463	301	8	201		408		208	363					255
20		Similarity (%)	76.4	74.9			73.5	57.7	89.0	53.0	736		44.4		51.4	51.5					74.9
		Identity (%)	42.8	43.4			47.2	34.3	67.4	49.0	40.8		26.7		25.0	27.0					51.8
25	ntinued)	gene	rculosis	rculosis			culosis	rans	licifer er1	APE0247	/aaE		enes ATCC		ia LaBelle- smid	amicum m) ATCC					er pur3
30	Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv3195	Mycobacterium tuberculosis H37Rv Rv3194			Mycobacterium tuberculosis H37Rv Rv3193c	Deinococcus radiodurans DR0840	Hevea brasiliensis laticifer er1	Aeropyrum pernix K1 APE0247	Bacillus subtilis 168 yaaE		Lysobacter enzymogenes ATCC 29487		Neurospora intermedia LaBelle- 1b mitochondrion plasmid	Corynebacterium glutamicum (Brevibacterium flavum) ATCC 17965 csp1					Strepto:nyces alboniger pur3
35		<u> </u>	ΣI	ΣI	<del> </del>	<del> </del>	ΣÏ	۵۵	ヹ	×	Ì	-	35	-	ž₽	7 (B)	_	$\vdash$	$\vdash$	-	क्र
40		db Match	pir.A70951	pir H70950			pir G70950	gp:AE001938_5	SP.ER1_HEVBR	PIR:F72782	sp:YAAE_BACSU		pir.TRYX94		pir. S03722	sp.CSP1_CORGL					рл.2207273Н
		OR⊤ (₽р)	1446	1050	675	522	2955	1359	951	345	900	363	1062	501	585	1581	429	510	222	309	780
45		Terminal (r.t)	822680	825239	825242	825996	829570	829627	831971	831578	832570	832795	834633	835388	835837	838892	839353	840139	840210	840437	841517
50		Initial (nt)	824125	824190	825916	826517	825616	830985	831021	831922	831971	833157	833572	834888	835253	837312	838925	839630	840431	840745	842296
		SEQ NO (a.a.)	4373	4374	4375	437¢	4377	4378	4379	4380	4381	4382	4383	4384	4385	4386	4387	4388	4389	4390	4391
55	. [	SEO NO (DNA)	873	874	875	976	877	878	979	$\neg$	881	882	983	884	885	986	887	888	688	068	89:

81

EP 1 108 790 A2

_							— т	<del></del>			-	<del></del>						
	Function	myo-inositol monophosphatase	peptide chain release factor 2	cell division ATP-binding protein	hypothetical protein	celi division protein	small protein B (SSRA-binding protein)	hypothetical protein				vibriobactın utilization protein	Fe-regulated protein	hypothetical membrane protein	ferric anguibactin-binding protein precursor	ferrichrome ABC transporter (permease)	ferrichrome ABC transporter (permease)	ferrichrome ABC transporter (ATP-binding protein)
	Matched length (a.a.)	243	359	226	72	301	145	116				272	319	191	325	313	312	250
	Similarity (%)	59.3	886	91.2	54.0	74.8	75.9	73.3				52.9	58.3	71.2	61.5	80.8	76.0	82.0
	Identity (%)	33.7	0.89	70.4	43.0	40.5	43.5	44.0				26.8	29.5	36.1	27.7	39.3	.35.6	48.4
Table 1 (continued)	Homologous gene	Streptomyces flavopersicus spcA	Streptomyces coelicalor A3(2) prfB	Mycobacterium tuberculosis H37Rv Rv3102c ftsE	Aeropyrum pernix K1 APE2061	Mycobacterium tuberculosis H37Rv Rv3101c flsX	Escherichia coli K12 smpB	Escherichia coli K12 yeaO				Vibrio cholerae OGAWA 395 ViuB	Staphylococcus aureus sirA	Mycobacterium leprae MLCB1243.07	Vibrio anguillarum 775 fatB	Bacillus subtilis 168 yclN	Bacillus subtilis 168 yclO	Bacillus subtilis 168 yclP
	db Match	gp:U70376_9	sp:RF2_STRCO	pir.E70919	PIR:G72510	pir.D70919	sp.SMPB_ECOLI	Sp:YEAO_ECOLI				Sp.VIUB_VIBCH	prf.2510361A	gp:MLCB1243_5	sp.FATB_VIBAN	pir B69763	pir.C69763	pir.D69763
	ORF (bp)	819	1104	687	264	900	492	351	537	300	405	825	918	588	1014	666	942	753
	Terminal (n:)	842306	844360	845181	844842	846097	846628	846982	846269	848026	847718	848499	849326	850412	852364	853616	854724	855476
	initial (nt)	843124	843257	844495	845105	845198	845137	845632	846805	847727	848122	849323	850243		851351	852618	853783	854724
	SEQ NO.	4392	4353	4394	4395	4396	4397	4398	4399	4400	4401	4402	4403	4404	4405	4406	4407	4408
	SEQ NO (DNA)	<del></del>	893	894	895		897	898	669	666	901	602	903	904	906	906	907	806

EP 1 108 790 A2

												,	,	_					
10	Function	hypothetical protein	hypothetica! protein	kynurenine aminotransferase/glutamine transaminase K		DNA repair helicase	hypothetical protein	hypothetical protein		resuscitation-promoting factor	cold shock prolein	hypothetical protein	glutamine cyclotransferase			permease		IrRNA(adenosine-2'-0-)- methy:transferase	
15	Matched length (a.a.)	48	84	442		613	764	27		198	61	159	273			477		310	
20	Similarity (%)	72.0	66.0	64.9		62.3	65.2	62.0		64.7	75.4	58.5	67.8			79.3		51.7	
	Identity (%)	66.0	61.0	33.5		30.7	36.1	44.0		39.4	42.6	28.3	41.8			43.6		27.9	
25 Table 1 (Continued)	Homologous gene	Chlamydia muridarum Nigg TC0129	Chlamydia pneumoriae	Rattus rorvegicus (Rat)		Saccharomyces cerevislae S288C YIL143C RAD25	Mycobacterium tuberculosis H37Rv Rv0862c	Mycobacterium tuberculosis H37Rv Rv0863		Micrococcus futeus rpf	Lactococcus lactis cspB	Mycobacterium leprae MLCB57.27c	Deinococcus radiodurans DR0112			Streptomyces coelicolor A3(2) SC6C5.09		Streptomyces azureus IsnR	
40	db Match	PIR:581737	GSP: Y35814	pir.S66270		sp:RA25_YEAST	pir F70815	pir G70815		prf.2420502A	prf.2320271A	gp:MLCB57_11	gp:AE001874_1		-	6_326C5_9		SP_TSNR_STRAZ	
	ORF (bp)	147	273	1209	639	1671	2199	219	843	597	381	525	774	669	138	1473	912	828	876
45	Termina' (nt)	860078	860473	862752	862753	863396	865119	867571	868630	e67803	869318	869379	869918	870721	871660	873210	872016	87404C	874269
50	Initia: (nt)	850224	850745	851544	853391	865068	867317	867353	867788	868399	868938	869903	870691	871419	871523	871738	872927	873213	874944
	SEQ NO (a a)	4409	4410	4411	4412	4413	4414	4415	44.6	4417	<u> </u>	44.9	4420	4421	4422	4423	4424	4425	4426
5 <i>5</i>	SEO NO DNA)	606	910	<del></del> -	912		914	915	515	917	918	919	920	921	922		924	925	926

EP 1 108 790 A2

														<del></del>	一丁		$\neg \tau$		$\neg \top$		
5		Function	hypothetical protein	phosphoserine transaminase	acetyl-coenzyme A carboxylase carboxy transferase subunit beta	hypothetical protein	sodium/proline symporter		hypothelical protein	fatty-acid synthase			homoserine O-acetyltransferase			glutaredoxin	dihydrofolate reductase	thymidylate synthase	аттопічт transporter	ATP dependent DNA helicase	formamidopyrimidine-DNA glycosidase
15		Matched length (a.a.)	316	374	236	103	549		243	3026			335			62	171	261	202	1715	298
20		Similarity (%)	55.1	52 9	69.5	80 6	58 1		77.4	83.4			59.7			72.6	62.0	88.9	56.4	68.1	51.0
		Identity (%)	32.6	21.9	36.0	51.5	26.4		49.0	63.1			29.0			43.6	38.0	64.8	32.2	47.4	29.2
25	ontinued)	s gene	ercuiosis	VTCC 21783	2 accD	icolor A3(2)	rescens		erculosis				metX			durans	ium folA	12 thyA	12 cysQ	licolor A3(2)	orgatus
30	Table 1 (continued)	Homologous gene	Mycobacterium tubercuiosis H37Rv Rv0883c	Bacillus circulans ATCC 21783	Escherichia coli K12 accD	Streptomyces coelicolor A3(2) SCIB.08c	Pseudomonas fluorescens		Mycobacterium tuberculosis H37Rv Rv2525c	Corynebacterium ammoniagenes fas			Leptospira meyeri metX			Deinococcus radiodurans DR2085	Mycobacterium avium folA	Escherichia coli K12 thyA	Escherichia coli K12 cysQ	Streptomyces coelicalar A3(2) SC7C7, 16c	Synechococcus elorgatus naegeli :nutM
35			<u>₹</u> £	88	S I	श्रु क्ष	P.	-	₹ E	2 2			의			ة ق	Σ̈́	ű	<u> </u>	ळ ळ	SE
40		db Match	sp:YZ11_MYCTU	pir:S71439	sp:AccD_EcoLI	gp:SCI8_8	pir.JC2382		pir.A70657	pir:S55505			prf.2317335B			gp:AE002044_8	prf:2408256A	SP.TYSY_ECOLI	sp:CYSQ_ECOLI	gp:SC7C7_16	sp.FPG_SYNEN
		ORF (bp)	933	1128	1473	339	:653	816	840	8907	489	186	1047	426	267	237	456	798	756	4560	768
45		Termina! (nt)	874951	875985	879642	881985	883647	884541	884549	894578	895191	895593	895596	896719	897689	897727	897979	898434	899253	904602	905382
50		Initial (nt)	875883	877112	88:114	881647	88.995	883726	885388	885672	894703	895408	896642	897144	897423	897963	898434	899231	800006	900043	904615
	•	SEQ NO	4427	4428	4429	4430	4431	4432	4433	4434	4435	4436	4437	4438	4439	4440	4441	4442	4443	4444	4445
55		SEO NO (INA)	126	928	+	930	931	932	933	934	935	936	937	938	939	940	941	942	T-	944	945

					<del></del>	<del></del>														
5 10		Function	hypothetical protein	alkaline phosphatase	integral membrane transporter		glucose-6-phosphate isomease	hypothetical protein		hypothetical protein	ATP-dependent helicase	ABC transporter	ABC transporter		peptidase	hypothetical protein		5'-phosphoribosylg'yoinamide formyltransferase	5'-phosphoribosyl-5-aminoimidazole-4-carboxamide formyltransferase	citrate lyase (subunit)
15		Matched length (a.a.)	128	196	403		557	195		78	763	885	217		236	434		189	525	217
<b>20</b>		Similarity (%)	86.7	71.9	67.0		77.0	52.3		85.9	73.1	48.6	71.4		73.3	60.8		86.2	87.8	100.0
		Identity (%)	55.5	38.8	33.8		52.4	24.6		59.0	46.1	21.8	43.8		43.6	31.1		64.6	74.5	100.0
30 35	Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv0870c	Lactococcus lactis MG1363 apl	Streptomyces coelicolor A3(2) SC128.06c		Escherichia coli JM101 pgi	Mycobacterium tuberculos's H37Rv Rv0336		Mycobacterium tuberculos:s H37Rv Rv0948c	Bacillus stearothermophilus NCA 1503 pcrA	Streptomyces coelicolor A3(2) SCE25.30	Bacillus subtilis 168 yvrO		Mycobacterium tuberculosis H37Rv Rv0950c	Mycobacterium tuberculosis H37Rv Rv0955		Corynebacterium ammoniagenes purN	Corynebacterium ammoniagenes purH	Corynebacterium glutamicum ATCC 13032 citE
40		ORF db Match	408 pir.F70816	600 sp.AP_LACLA	1173 pir T36776	717	1620 pir.NUEC	1176 pir.G70506	381	309 sp:YT26_MYCTU	2289 sp:PCRA_BACST	2223 gp:SCE25_30	666 prf.2420410P	507	711 pir.D73716	1425 sp:YT19_MYCTU	228	627 gp AB003159_2	1560 gp:AB003159_3	819 gp:CGL133719_3
45		Terminal O	905796 4	905792 6	906559 11	909328 7	907759 16	909521	911223 3	910855 30	913514 22	913477 22	915699 66	916368 5(	916970 7	919352 14	917827 22	919956 62	921526 15	922412 81
50		Initial (nt)	905389	906391	907731	908612	903378	910696	910843	911163	911226	915699	915364	916874	917680	917928	918054	919330	919967	921594
		SEO NO.	4446	4447	4448	4449	4450	4451	4452	4453	4454	4455	4456	4457	4458	4459	4460	4461	4462	4463
<i>55</i>		SEQ NO.	946	547	649	649	950	951	525	953	954	955	956	957	928	626	7 396	961 4	962	963

EP 1 108 790 A2

· .	Function	repressor of the high-affinity (methyl) ammonium uptake system	hypothetical protein	9	30S ribosomal protein 3 to	30S ribosomal protein 514	50S ribosomal protein L33	50S ribosomal protein L28	transporter (sulfate transporter)	Zn/Co transport repressor	50S ribosomal protein L31	50S ribosomal protein L32		copper-inducible two-component regulator	two-component system sensor	proteinase DO precursor	molybdopterin biosynthesis cnx1 protein (molybdenum cofactor biosynthesis enzyme cnx1)		large-conductance mechanosensitive channel	hypothetical protein	5-formyltetrahydrofolate cyclo-ligase
	Matched length (a.a.)	222	109		/9	130	49	77	529	80	78	55		227	484	406	188		131	210	191
	Similarity (%)	100.0	100.0		76.1	80.0	83.7	81.8	71.1	77.5	65 4	78.2		73.6	60.1	59.9	54.3		77.1	60.0	59.7
	Identity (%)	100.0	100.0		52.2	540	55.1	52.0	34.4	37.5	37.2	0.09		48.0	24.4	33.3	27.7		50.4	28.6	25.1
Table 1 (continued)	Homologous gene	Corynebacterium glutamicum ATCC 13032 amtR	Corynebacterium glutamicum ATCC 13032 yjcC		Cyanophera paradoxa rps18	Escherichia coli K12 rpsN	Escherichia coli K12 rpmG	Escherichia coli K12 rpmB	Bacillus subtilis 168 yvdB	Staphylococcus aureus zntR	Haemophilus ducreyi rpmE	Streptomyces coelicolor A3(2) SCF51A: 4		Pseudomonas syrirgae copR	Escherichia coli K12 baeS	Escherichia coli K12 htrA	Arabidopsis thaliana CV cnx1		Mycobacterium luberculosis H37Rv Rv0985c mscL	Mycobacterium tuberculosis H37Rv Rv0990	Homo sapiens MTHFS
	db Match	gp.CGL133719_2	gp:CGL133719_1		sp:RR18_CYAPA	sp.RS14_ECOLI	sp:RL33_ECOLI	pir:R5EC28	pir.B70033	pr: 2420312A	Sp.RL31_HAEDU	gp:SC51A_14		sp.COPR_PSESM	sp.BAES_ECOLI	pir:S45229	sp:CNX1_ARATH		sp:MSCL_MYCTU	pir.A70601	pir.JC4389
	ORF (bp)	999	327	321	249	303	162	234	1611	312	264	171	447	969	1365	1239	585	198	405	651	670
	Terminal (nt)	922396	923138	923981	924159	924425	924734	924901	925325	926931	927737	927922	927339	928812	930248	931648	932290	932487	932570	933060	933733
	Initial (nt)	923061	923464	923661	924407	924727	924895	925134	926935	927242	927474	927752	927785	928117	928884	930410		932290	<del></del>	933710	934302
	SEQ	4464	4465	4456	4457	4458	4469	4470	4471	4472	4473	4474	4475	4476	4477	4478	4479	4480	4481	4482	4483
	SEQ.	964 4464	965	996	296	996	696	T	971	972	973	974	975		977	978	626	980	981	982	983

				T		_						-,						
5	Function	UTP-glucose-1-phosphate uridyly transferase	molybdopterin biosynthesis protein	ribosomal-protein-alanine N- acetylt:ansfe:ase	hypothetical membrane protein	cyanate transport protein		hypothetical membrane protein	hypothetical membrane protein	cyclomaltodextrinase	hypothetical membrane protein	hypothetical protein	methionyl-tRNA synthetase	ATP-dependent DNA helicase	hypothetical protein	hypothetical protein		transposase
15	Matched length	(a.a.) 296 U	390 m	193 rib	367 ћу	380 cv	<b>†</b>	137 hy	225 hy	444 Cyt	488 hy	272 hyp	615 me	741 AT	210 hyp	363 hyp	-	94 tran
20	Similarity	689	62.5	549	54 8	62.4	-   	9.09	59.6	53.6	75.2	78.3	66.7	49.0	53.3	59.0		59.6
	Identity (%)	42.2	31.8	29.0	30.3	26.6		32.1	25.3	26.8	43.0	54.0	33.8	26.2	27.6	30.0		33.0
25	(nar		S		sis			22	S. S.		.si	sis	I		Ξ			
	Homologous gene	Xanthomonas campestris	Arthrobacter nicotinovorans mceA	Escherichia coli K12 rimJ	Mycobacterium tuberculosis H37Rv Rv0996	Escherichia coli K12 cynX		Haemophilus influenzae Rd H1602	Mycobacterium tuberculosis H37Rv Rv0093c	Bacillus sphaericus 5-244 CDase	Mycobacterium tuberculosis H37Rv	Mycobacterium tuberculosis H37Rv Rv1003	Methanobacterium thermoautotrophicum Delta H MTH587 metG	Escherichia coli recQ	Methanobacterium thermoautotrophicum Delta H MTH796	Bacillus subtilis 168 yxaG		Enterococcus faecium
35		×	∢ E		ΣI				·-·-		ΣÏ			ŭ	ΣŞΣ		_	
40	db Match	pir.JC4985	prf:2403296B	SP:RIMJ_ECOL:	pir:G73601	Sp.CYNX_ECOLI		sp:YG02_HAEIN	sp:Y05C_MYCTU	sp:CDAS_BACSH	pir.E70602	sp.Y19J_MYCTU	SP.SYM_METTH	prf. 1336383A	pir.B69206	sp:YXAG_BACSU		gp.AF029727_1
	ORF (bp)	897	1257	099	1020	1200	1419	405	714	1167	1560	825	1830	2049	633	1158	531	294
45	Termina! (nt)	935319	9366C7	937274	938401	939626	937799	940090	940754	941925	942381	944833	948669	950839	950828	951834	953043	954266
50	In:tia' (nt)	934423	935351	936615	937382	938427	939217	939686	943041	940759	943940	944009	946840	948791	951460	952991	953573	953973
	SEQ NO	<del>+</del>	4485	4486	4487	4468	4489	4490	4491	4492	4493	4494	4495	4496	4497	4458	4499	4500
55	SEC NO SNO	984	985	986	987	988	989	C66	991	266	993	994	995	966	266	866	666	80.

87

EP 1 108 790 A2

	Function	transposase	transposase subunit		D-lactate dehydrogenase	site-specific DNA-methyltransferase		transposase	transposase	transcriptional regulator	cadmium resistance protein		hypothetical protein	hypothetical protein	dimethyladenosine transferase	isopentenyl monophosphate kinase		ABC transporter	pyridoxine kinase	hypothetical protein	hypothetical protein
	Matched length (a.a.)	139	112		565	231		98	139	91	205		263	362	265	315		478	242	159	108
	Similarity (%)	9.79	88.4		75.6	62.8		59.6	9.79	84.6	8.99		7.07	63.5	65.3	67.0		85.8	67.4	58.5	78.7
	Identity (%)	- 41.7	73.2		46.4	30.8		33.0	41.7	62.6	31.7		46.4	34.8	34.3	42.5		65.5	40.1	27.0	45.4
Table 1 (continued)	Homologous gene	Escherichia coli K12	Brevibacterium linens tnpA		Escherichia coli did	Kiebsiella pneumoniae OK8 kpn!M		Enterococcus faecium	Escherichia coli K12	Mycobacterium tuberculosis H37Rv Rv1994c	Staphylococcus aureus cadD		Mycobacterium tuberculosis H37Rv Rv1008	Mycobacterium tuberculosis H37Rv Rv1009 rpf	Escherichia coli K12 ksgA	Mycobacterium tuberculosis H37Rv Rv1011		Saccharopolyspora erythraea ertX	Escherichia coli K12 pdxK	Mycobacterium tuberculosis	Streptomyces coelicolor A3(2) SCF1.02
	db Match	pir TOEC13	1 22		1713 prf.2014253AE	Z		gp AF329727_1	Ī <sup>—</sup>		prf.2514367A		pir C73603	pir.D72603	Sp.KS3A_ECOLI	933 pir.F70603		3 pir.S47441	SP PDXK ECOLI		21 gp.SCF1_2
	OR (gd)	47.7	414	864	1713	840	219	294	477	357	621	342	831	1071	879	933	642	1833	792	1	1 6
	Terminal (nt)	054753	955354	956774	955686	957844	959185	960374	960961	961653	962249	961321	963639	964934	965852	966784	965950	968660	969458	969461	970349
	Iritial (1t)	054277	054041	955911	957398	953683	959403	960081	960385	961297	961629	961662	962809	963864	964974	965852	965591	966828	968667	<u> </u>	970029
	SEQ	÷	<del>-</del> -	<del>_</del>			4506	4507	4508	4509	45:0	4511	4512	4513	45.4	4515	4516	4517	4518	4519	1020 4520
	SEQ						1006	<del></del> -	<del>-i</del>		1010	10.1	10.2	1013	1314	1015	1016	1017	101	1019	1020

					_															
5		Function	tein			lein	ilase			major secreted protein PS1 protein precursor	gulator (tetR	out protein	onine:2-		. <u>c</u>	.c			ase factor 3 ort protein	
10			hypothetical protein	requistor		hypothetical protein	andu voo doub			major secreted p	transcriptional regulator (tetR	ramily ) membrane fransport protein	S-adenosylmethionine.2-demethylmenaquinone	methyltransferase	hypothetical protein	hypothetical protein			amide-urea transport protein	
15	•	2 -	(a.a.)	261		337				440	100	1	157		121	482	十	7,46	1	
20		Similarity (%)	69.2	88.1		70.9				56.8	70.0	70.0	75.8	T	63.6	48.3	1	0 89	72.8	
		Identity (%)	35.5	64.8	27,	35.6				27.7	44.0	42.6	38.2		29.8	24.9		30.7	42.8	1
25	(pend	)   	r A3(2)	A3(2)		osis				icum ATCC	A3(2)	A3(2)	2		AA1953	sis	7		Shus	
30	Table 1 (continued)	Homologous gene	Streptomyces coelicolor A3(2) SCF1.02	Streptomyces coelicolor A3(2)	Bacillus subtilis 168 vveH	Mycobacterium tuberculosis H37Rv echaq				Corynebacterium glutamicum (Brevibacterium flavum) ATCC 17965 csp1	Streptomyces coelicolor A3(2) SCF56.06	Streptomyces coelicolor A3(2) SCE87, 17c	Haemophilus influenzae Rd H10508 menG		Neisseria meningitidis NMA1953	Mycobacterium tuberculosis H37Rv Rv1128c		Escherichia coli K12 prfC	Methylophilus methylotrophus fmdD	
35			Strep	Strep	1	Myco H37R		_	_	Coryn (Brevi 17965	Strept SCF56	Strept	Нает Н1050		Neisse	Mycob H37Rv		Escher	Methylc	
40		F db Match	gp:SCF1_2	gp:SCJ1_15	sp:YXEH_BACSU	pir.E7C893				sp:CSP1_CORGL	gp:SCF56_6	gp:SCE87_17	SP:MENG_HAEIN		gp:NMA622491_21	pir.A70539		pir:159305	prf:2405311A	
45		R d	321	096	792	1017	654	111	1212	1385	579	2373	498	999	381	1551	936	1547	1269	
		Terminal (nt)	970738	971823	972244	974155	973304	974962	974965	977734	977800	978368	981493	982287	982294	984650	985845	984864	988007	
50		Initial (nt)	370418	370864	973035	973139	973957	974186	376176	976349	978378	980740	980993	98 1622	982674	983100	984910	986510	986739	
	- از ترسس	NO (a a)	4521	4522	4523	4524	4525	4526	4527	4528	4529	4530	4531	4532	4533	4534	4535	4536	4537	
55		SEQ NO (DNA)	1021	1022	1023	1024	1025	1026	1627	1029	1029	1030	1031	1032	1033	<del></del>	. —÷	1036	1037	

						-								i i	i	1	- 1	- 1	1
5		Function	sport protein	sport protein	high-affnity branched-chain amino acid transport ATP-binding protein	high-affinity branched-chain amino acid transport ATP-binding protein	drolase	lioxygenase	3-phosphate	polypeptides predicted to be useful antigens for vaccines and diagnostics	ydrolase	irotein L25	e lyase	epair enzyme	le ase	ucosamine ase		cursor	nodulation ATP-binding protein I
10		Fu	amide-urea transport protein	amide-urea transport protein	high-affinity bran acid transport A	high-affinity branacid transport A	peptidyl-tRNA hydrolase	2-nitropropane dioxygenase	glyceraldehyde-3-phosphate dehydrogenase	polypeptides predicted to antigens for vaccines and diagnostics	peptidyi-tRNA hydrolase	50S ribosomal protein L25	lactoylglutathione lyase	DNA alkylation repair enzyme	ribose-phosphate pyrophosphokinase	UDP-N-acetylglucosamine pyrophosphorylase		sufl protein precursor	nodulation ATP
15		Matched length (a.a.)	77	234	253	236	187	361	342	51	174	194	143	208	3.6	452		206	310
20		Similarity (%)	61.0	68.0	0.07	69.1	706	540	72.8	61.0	63.2	65.0	546	62.5	79.1	71.9	-	61.7	64.8
		identity (%)	40.8	34.6	37.9	35.2	39.0	25.2	39.5	54.0	38.5	47.0	28.7	38.9	44.0	42.0		30.8	35.8
25 9 1	initiaca)	gene	ılotrophus	Aotrophus	ginosa PAO	ginosa PAO	pth	0895	deg snyln)	1s	2 pth	ercu!osis	num D21	CC 10987		٥	,	2 suf	lpou
30 tolder	ומחוב ו	Homologous gene	Methylophilus methylotrophus fmdE	Methylophilus methylotrophus fmdF	Pseudomoras aeruginosa PAO braF	Pseudomonas aeruginosa PAO braG	Escherichia coli K12 pth	Williopsis mrakii IFO 0895	Streptomyces roseofulvus gap	Neisseria meningitid s	Escherichia coli K12 pth	Mycobacterium tubercutosis H37Rv rplY	Salmonella typhimurium D21 gloA	Bacillus cereus ATCO 10987 alkD	Bacillus subtilis prs	Bacillus subtilis gcaD		Escherichia coli K12 sufl	Rhizobium sp. N33 nodl
<b>35</b> <b>40</b>		db Match	prf:2406311B	prf:2406311C	SP.BRAF_PSEAE	sp:BRAG_PSEAE	SD:PTH ECOLI	SP. 2NPD WILMR	sp.G3P_ZYMMO	GSP-Y75094	SP.PTH ECOLI	pir.B70622	sp:LGUL_SALTY	prf.2516401BW	sp.KPRS_BACCL	pir.S66080		Sp.SUFI_ECOLI	
		ORF (bp)	882	1077	726	669	612		1065	369	531	909	429	524	975	1455	1227	1533	918
45		Terminal (nl)	988904	086980	990705	991414	991417	993080	994613	994106	994845	995527	996830	996833	997466	998455	1000016	.1	
50	İ	Initial (nt)	988023	988904	086686	990716	992028	992058	993549	994474	995375		996402	997456	998440	606666	1001242	1	
		SEQ NO.	4538	4539	4540	4541	4542	4543	4544	4545	4546	4547	4548	4549	4550	4551	4552		
55		SEQ NO. (DNA)		1039	1040	1041	1042			1045	1046	1047	1048	1049	1050	1051	1052	1053	1054
_	- 1	<u> </u>		<del></del>	т—				<del></del> -									_	_

5	Function	hypothetical membrane protein	two-component system sensor histidine kinase	two component transcript onal regulator (luxR family)		hypothetical membrane protein	ABC transporter		ABC transporter	gamma-g!utamyltranspeptidase precursor					transposase protein fragment	transposase (1S1628 TnpB)				transcriptional regulator (TetR- family)	transcription/repair-coupling protein	
15	Matched length (a.a.)	272	459	202		349	535		573	999					37	236				183	1217	
20	Similarity (%)	63.2	48.4	67.3		64.5	57.0		74.C	58.6					72.0	100.0				59.6	65.1	
	Identity (%)	30.2	24.6	36.6		31.5	28.6		44.0	32.4				_	64.0	9.66				23.0	36.2	
25 Table 1 (continued)	Homologous gene	vidans ORF2	K12 uhpB	eucetius dnrN		oelicolor A3(2)	Streptomyces glaucescens strV		Mycobacterium smegmatis exiT	i K12 ggt					Corynebacterium glutamicum TnpNC	Corynebacterium glutamicum 22243 R-plasmid pAG1 tnpB				ii tetR	li mfd	
735 Table	Hemolog	Streptomyces I vidans ORF2	Escherichia coli K12 uhpB	Streptomyces peucetius dnrN		Streptomyces coelicolor A3(2) SCF15.07	Streptomyces		Mycobacterium	Fscherichia coli K12 ggt						Corynebacteriu 22243 R-plasm		`		Escherichia coli tetR	Escherichia coli mfd	
40	db Match	pir JN0853	sp:UHPB_ECOLI	pri.2107255A	-	gp:SCF15_7	pir.S65587		pir.T14180	sp.GGT_ECOL'					GPU.AF164956_23	gp.AF121030_8			-	sp.TETC_ECOU	SP MFD_ECOLI	
	ORF (bp)	831	1257	609	204	1155	1440	153	1734	1965	249	519	192	606	243	708	462	597	312	651	3627	1224
45	Terminal (nt)	1004793	1006095	1006697	1006734	1008152	1010061	1008534	1011790	1011797	1014264	1014343	1015116	1016560	1015450	:015145	1017018	1017274	1018393	1019066	1022715	1019390
50	Initial (nt)	1003953	1004829	1006039	1006937	4559 1006998	1008522	1008586	4562 1010057	1013761	1014016	1014861	1014925	1015652	10:5692	1015852	10.6557	1017870	1018082	1018416	4574 1019090	1020613
	SEQ NO.	+		4557	4558	4559	4560	4561	4562	4563	4564	4565	4566	4567	4568	4569	4570	4571	4572	4573	<del></del>	4575
55	SEQ NO	1055	1056	1357	1058	1059	1060	1361	1062	1063	1064	1065	1066	1067	990,	1069	1070	1071	1072	1073	1074	1075

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

Table 1 (continued)

_					<del></del>			—	- 1						1			$\overline{}$
	Function	Neisserial polypeptides predicted to be useful antigens for vaccines and diagnostics	multidrug resistance-like ATP- binding protein, ABC-type transport protein	ABC transporter	hypothetical membrane protein		hypothetical protein			IpqU protein	enolase (2-phosphoglycerate dehydratase)(2-phospho-D- glycerate hydro-lyase)	hypothetical protein	hypothetical protein	hypothetical protein	guanosine pentaphosphatase or exopolyphosphatase		threonine dehydratase	
	Matched length (a.a.)	92	632	574	368		183			241	422	41	191	153	329		314	
	Similarity (%)	0.69	62.7	81.9	100.0		57.4			689	86.0	58.0	55.0	77 8	55.0		64.7	
	Identity (%)	48.0	31.3	50.2	100.0		33.4			46.5	64.5	68.0	31.9	5.65	25.2		30.3	
(2011)	Homologous gene	Neisseria gonorrhoeae	Escherichia coli mdlB	Mycobacterium tuberculosis H37Rv Rv1273c	Corynebacterium glutamicum ATCC 13032 orf3		Bacillus subtilis yabN			Mycobacterium tuberculosis H37Rv Rv1022 lpqU	Bacillus subtilis eno	Aeropyrum pernix K1 APE2459	Mycobacterium tube culosis H37Rv Rv1024	Mycobacterium tuberculosis H37Rv Rv1025	Escherichia coli gppA		Escherichia coli tdc5	
	db Match	GSP:Y75301	sp:MDLB_ECOL!	sp.YC73_MYCTU	sp.YLI3_CORGL		sp.YABN_BACSU			pir:A70623	sp:ENO_BACSU	PIR:872477	pir:C70623	pir:D70623	sp:GP3A_ECOLI		sp:THD2_ECOLI	 
	ORF (bp)	228	1968	1731	2382	297	585	426	378	786	.275	144	540	546	963	984	930	195
	Terminal (nt)	1021078	1022699	1024566	1026505	103218	1032780	1032760	1333269	1034739	1036223	1036016	1036855	1037445	1038410	1036498	1038721	1039977
	Initial (nt)	1021305	1024666	1025396	1028886	1031885	1032196	1033185	1033646	1033954	1034949	1036159	1036316	1036900	1037448	1037461	1039650	1039783
	SEQ NO (a.a.)	4576	4577	4578	4579	4580	4581	4582	4583	4584	4585	4585	4587	4588	4589	4590	4591	4592
	SEQ NO. (DNA)	1076	1077	1078	1079	1090	108	1082	1083	1084	1085	1086	1067	1088	1089	1090	1091	1092

92

	- 1								$\overline{}$								$\neg \neg$					
5		oo			r of L-rhamnose				ion factor		<b>L</b>		neptulosonate-7-		or undecaprenyl Jetase					/I transferase	1 synthase	
10		Function		hypothetical protein	transcription activator of L-rhamnose operon	hypothetical protein		hypothetical protein	transcr ption elongation factor	hypothetical protein	lincomycin-production		3-deoxy-D-arabino-heptulosonate-7- phosphate synthase		hypothetical protein or undecaprenyl pyrophosphale synthetase	hypothetical protein			pantothenate kinase	serine hydroxymethyl transferase	p-aminobenzoic acid synthase	
15		Matched length (a.a.)		99	242	282		140	. 143	140	300		367		97	28			308	434	969	
20		Similarity (%)		74.1	55.8	1.08		57.1	60.1	72.1	56.3		99.5		97.3	100.C			79.9	100.0	70.1	
		Identity (%)		46.3	24.8	57.8		30.0	35.0	34.3	31.7		99.2		96.0	100.0			53.9	99.5	47.6	
25	ntinued)	gene		a MSB8	ď	rculosis		olor A3(2)	4	rculosis	nensis ImbE		utamicum		utamicum	utamicum um)			A	ım MJ-233	Sqed sr	
30	Table 1 (continued)	Homologous gene		Thermotoga maritima MSB8	Escherichia coli rhaR	Mycobacterium tuberculosis H37Rv Rv1072		Streptomyces coelicolor A3(2) SCF55.39	Escherichia coli greA	Mycobacterium tuberculosis H37Rv Rv1081c	Streptomyces lincolnensis ImbE		Corynebacterium glutamicum aroG		Corynebacterium glutamicum CCRC18310	Corynebacterium glutamicum (Brevibacterium flavcm)			Escherichia coli coaA	Brevibacterium flavum MJ-233 glyA	Streptomyces griseus pabS	
35				=		ΣÏ				ΣÏ	<i>I</i>								ECOLI E	<u> </u>		
40		db Match		pir. 972287	SP RHAR_ECOLI	pir.F7C893		gp:SCF55_39	sp.GREA_ECOLI	pir:G70894	pir:S44952		sp:AROG_CORGL		sp:YARF_CORGL	SP:YARF_CORGL			sp.COAA_EC	gsp:Re7745	sp:PABS_STRGR	
		ORF (bp)	330	189	993	816	387	450	522	483	873	318	1098	633	675	174	519	318	936	1302	1860	723
45		Terminal (nt)	1040325	1040682	1041917	1042842	1042850	104329B	1043/74	1044477	1046330	1046390	1047707	1046820	1048501	1048529	1049043	1049068	1049427	1051925	1053880	1054602
50		In:tial (nt)	1039595	1040494	1040925	1042027	1043236	.043747	.044295	.044959	.045158	.046073	.045610	.047452	-047827	.048356	.048525	1049385	1053362	.050624	1052021	4612 .053880
		SEQ NO.	4593	4594	4595	4596	4597	4598	4599	4600	4601	4602	4603	1604	4605	4605	4607	4608	4609	4610	4611	
55		SEQ NO.	1093	1094	1095	1095	1097	1098	1099	1:00	1101	1102	1103	1104	1105	1 106	1107	1108	1109	1110	1111	1112

EP 1 108 790 A2

5		Function			phosphinothricin resistance protin	hypothetical protein		hypothetical protein	lactam utilization protein	hypothetical membrane protein			transcriptional regulator		fumarate hydratase precursor	NADH-dependent FMN oxydoreductase			reductase	dibenzothiophene desulfurization enzyme A	dibenzothiophene desuffurization enzyme C (DBT sulfur dioxygenase)	dibenzothiophene desulfurization enzyme C (DBT sulfur dioxygenase)		
15		Matched length (a.a.)			165	300		225	276	165			204		456	159			184	443	372	391		
20		Sirrilarity (%)			58.8	59.0		57.8	52.2	81.2			63.2		79.4	65 4			810	2.78	51.3	61.6		
		Identity (%)			30.3	30.3		37.8	30.8	40.6			26.0		52.0	32.7			55.4	39. '	25.8	28.9		
<b>25</b>	ed)	_													Hwn	v			A3(2)	soxA	soxC	soxC		
	Table 1 (continued)	Homologous gene			Atcaligenes faecalis otcR	Escherichia coli ybgK		Escherichia coli ybgJ	Emericella nidulans lamB	Bacillus subtilis ycsH			Bacillus subtilis ydhC		Rattus norvegicus (Rat) fumH	Rhodococcus erythropolis IGTS8 dszD			Streptomyces coelicator A3(2) StAH10.16	Rhodacoccus sp. IGTS8 soxA	Rhodococcus sp. IGTS8 soxC	Rhodococcus sp. IGTS8 soxC		
35 40		dɔ Match			gp.A0*504_1	sp:YBGK_ECOLI		sp.YBGJ_ECOLI	SP. LAMB_EMENI	sp:YCSH_BACSU [6			SP.YDHC_BACSU		SP FUMH_RAT	gp.AF048979_1			gp:SCAH10_16	sp.SOXA_RHOSO	sp.SOXC_RHOSO	sp:SOXC_RHOSO		
		ORF (bp)	864	393	537 gp./	879 sp:`	1056	.ds 8b.	756 sp.1	591 sp:	572	603	681 sp.	.278	1419 sp	489 gp	261	447	564 gp.	1488 sp.	1080 sp.	1197 sp:	780	069
45		Terminal (	1055722	1054640	1056319	1056322	1058628 1	1057200	1057843	1958624	1059889	1059962	1060792	1062146	1062211	1064424	1064478	1064754	1065304	1067570	1068649 1	1069845	1068913	1069119
50		Initial (nt)	1054859	1055032	1055783	4616 1057200	1057573	1057868		1059214	1059218	1059360	4623 1060112	4624 1060869	1063629	4625 1063936	1064738	1065200	1065867	1066083	1067570	1068649	1069692	1069838
		SEQ NO (a a.)	4613	4614	4615		4617	4618	4619	4620	4621	4622		+	4625		4627	4628	4629	4630	4631	4632	4633	4634
55		SEO NO (DNA)	1113	1114	1115	1116	1117	1118	1119	1120	1121	1122	1123	1124	1125	1126	1127	1128	1129	1130	1131	1132	1133	1134

5		uc	atic e						Ē	E)		5					Ë	Ī		T	
		1 .=	alipha Jenas					ux protein	se small sub	se large sub		ed to be user s and				roline	in PS1 prote		protein	ansferase	
10		Function	FMN:H2-dependent aliphatic sulfonate monooxygenase	glycerol metabolism	hypothetical protein	hypothetical protein		transmembrane efflux protein	exodeoxyribonuclease small subunit	exodeoxyribonuclease large subunit	penicillin tolerance	polypeptides predicted to be useful antigens for vaccines and diagnostics		permease		sodium-dependent proline transporter	major secreted protein PS1 protein precursor	GTP-binding protein	virulence-associated protein	ornithine carbamoylt ansferase	hypothetical protein
15		Matched length (a a)	397	325	211	227		82	29	466	311	131		338		552	412	361	75	30.	143
20		Similarity (%)	73.1	75.7	56.4	66.1		78.1	67.7	55.6	78.8	47.0		63.9		61.4	0.09	9.88	0.08	58.8	6.69
		Identity (%)	45.3	44.3	27.5	31.3		36.6	40.3	30.0	50.2	33.0		26.3		30.3	29.9	70.1	57.3	29.6	39.2
25	nued)	ne	On	Χď	losis			r A3(2)	31655	31655	В			ž		SLC6A7	nicum ATCC		intA	sa argF	8
30	Table 1 (continued)	Homologous gene	Escherichia coli K12 ssuD	Escherichia co'i K12 glpX	Mycobacterium tuberculosis H37Rv Rv1100	Bacillus subtilis ywmD		Streptomyces coelicolor A3(2) SCH24.37	Escherichia coli K12 MG1655 xseB	Escherichia col: K12 MG1655 xseA	Escherichia coli K12 lytB	Neisseria gonorrhoeae		Escherichia coli K12 perM		Rattus norvegicus (Rat) SLC6A7 ntpR	Corynebacterium glutamicum (Brev:bacterium f!avum) ATCC 17965 csp1	Bacillus subtilis yyaF	Dichelobacter nodosus intA	Pseudomonas aeruginosa argF	Bacillus subtilis 168 ykkB
35					H <sub>3</sub>	Ва		Str				Z				Rattu ntpR		- 1			Í
40		db Match		Sp.GLPX_ECOU	pir.B70897	pir:H70062		gp:SCH24_37	sp:EX7S_ECOLI	sp:EX7L_ECOLI	sp:LYTB_ECOLI	GSP:Y75421		SP. FERM_ECOLI		sp:NTPR_RAT	sp:CSP1_CORGL	sp:YYAF_BACSU	sp:VAPI_BACNO	SP.OTCA_PSEAE	sp:YKKB_BACSU
		(pp)	1176	963	570	1902	285	225	243	1251	975	429	828	1320	180	1737	1233	1083	297	822	501
45		Terminal (nt)	1071134	1071479	1073245	1073340	1075641	1075329	1075667	1075933	1078271	1077306	1078319	1079221	1080786	1080972	1082951	1085462	1086087	1086917	1087044
50		In tiat (nt)	1069959	1072441	1072676	1075241	1075357	1075553	1075909	1077183	1077297	1077734	4645 1079145	1080540	1080965	1082708	4649 1084183	4650 1084380	4651 1085791	1086095	4653 1087544
		SEO NO (a a)	4635	4636		1638	4639	4640	4641	4642	4643	1144 4644		4648	4647	4649		4650	4651		
55		SEQ NO (DNA)	1135	1.36	1:37	1138	1139	.140	:141	1142	:143	1144	1145	1146	1147	1148	1149			1152	1153

EP 1 108 790 A2

	_													_					
5		Function	9-cis retinol dehydrogenase or oxidoreductase	transposase/integrase (IS110)	hypothetical membrane protein	N-acetylglucosaminyltransferase			fransposase (insertion sequence IS31831)	transposase	transposase				oxidoreductase or morpyine-6- dehydrogenase (naloxone reductase)	4-carboxymuconolacione decarboxiyase			frenolicin gene cluster protein involved in frenolicin biosynthetic
15		Matched length (a.a.)	198 9-	396 tre	1153 hy	259 N			97 tra	125 tre	48				264 de	108 de			146 fr
20		Similarity (%)	9.09	73.0	52.2	47.1			93.8	94.4	95.8				66.3	63.9			66.4
		Identity (%)	33.8	42.2	23.0	22.8			82.5	79.2	87.5				37.5	33.3			34.9
25	(juned)	jene		ilor	yegE	dC dC			amicum	tamicum fermentum)	lamicum fermentum)				M10 norA	ceticus			ulvus frnS
30	Table 1 (continued)	Homologous gene	Mus musculus RDH4	Streptomyces coelicolor SC3C8.10	Escherichia coli K12 yegE	Rhizobium meliloti nodC			Corynebacterium glutamicum ATCC 31831	Corynebacterium glutamicum (Brevibacterium lactofermentum) ATCC 13869	Corynebacterium glutamicum (Brevibacterium lactofermentum) ATCC *3869				Pseudomonas putida M10 norA	Acinetobacter calcoaceticus dc4c			Streptomyces roseoʻulvus frnS
35 40		db Match	gp:AF013289_1	sp:YIS1_STRCO	sp:YEGE_ECOLI	SP.NODC_RHIME			pir.S43613	pir.JC4742	pir.JC4742				sp:MORA_PSEPU	sp.DC4C_ACICA			gp:AF056302_19
		ORF (tp)	630	1206	3042	765	219	333	291	375	144	141	366	498	843	321	663	195	654
45		Terminal (n:)	1087664	1088535	1093216	1094693	1094911	1095384	1095387	1095719	1096188	1096331	1096746	1097726	1098592	1098929	1099750	1099015	1099115
50		Initial (nt)	1088293	1089740	1090175	1093929	1094693	1095052	4660 1095677	1096093	1096331	1096471	1097111	1097229	1097750	1098609	1099088	1099209	4670 1099768
		SEQ NO.	+	4655	4656	4657	4658	4659	4660	4661	4662	4663	4664	4665	4666	4667	4658	4659	
55		SEQ. 100	-+	1155	1156	1157	1158	1159	1160	1161	1162	1163	1164	1165	1166	1167	1168	1169	1170

				_	T	<del></del>		_											
5		Function	biolin carboxylase						hypothetical protein	magnesium chelatase subunit	2,3-PDG dependent phosphoglycerate mutase	hypothetical protein	carboxyphosphonoenolpyruvate phosphonomutase	tyrosin resistance ATP-binding protein	hypothelical protein	alkylphosphonate uptake protein	transcriptional regulator	multi-drug resistance efflux pump	transposase (insertion sequence IS31831)
15		Matched length (a.a.)	563						655	329	160	292	248	593	136	E	134	367	436
20		Similarity (%)	78.5						80.3	52.6	62.5	60.7	59.3	54.1	6.99	82.0	62.7	59.4	8.66
		Identity (%)	48.1			_			57.9	27.7	33.8	38.2	29.4	31.7	29.4	55.0	32.1	22.6	99.5
30	lable 1 (continued)	Homologous gene	Synechococcus sp. PCC 7942 accC						Mycobacterium tuberculosis H37Rv Rv0959	Rhodobacter sphaeroides ATCC 17023 bchl	Amycolatopsis methanolica pgm	Mycobacterium tuberculosis H37Rv Rv2133c	Streptomyces hygroscopicus SF1293 BcpA	Streptomyces fradiae ttrC	Mycobacterium tuberculosis H37Rv Rv2923c	Escherichia coli K12 MG1655 phnA	Bacillus subtilis 168 yxaD	Streptococcus pneumoniae pmrA	Corynebacterium glutamicum (Brevibacterium lactofermentum) ATCC 31831
40		db Match	gp:SPU59234_3						SP.YT15_MYCTU	sp:BCHI_RHOSH	gp:AM:J73808_1	pir.A70577	gp:STMBCPA_1	sp:TLRC_STRFR	sp:Y06C_MYCTU	sp.PHNA_ECOLI	sp:YXAD_BACSU	gp:SPN7367_1	pir.S43613
		ORF (bp)	1737	597	498	345	153	639	1956	1296	642	705	762	1641	396	342	474	1218	1308
45		Terminal (nt)	1101653	1102639	1103192	1103524	1104103	1105561	1104103	1106086	1108201	1108905	1109754	1111432	1111425	1112230	1112484	1114319	1115793
50		Initial (nt)	1099917	1102043	1102695	1103180	1103951	1104923	1106058	110738:	1107560	1108201	1108993	1109792	11:1820	1111889	1112957	1113102	1114486
	İ	SEQ NO.	4671	4672	4673	4674	4575	4676	4677	4678	4679	4680	4681	4682	4683	4684	4685	4586	4687
55		SEO NO (DNA)	1171	1172	1173	1174	1175	1176	1177	1178	1179	1180	11811	1182 4	1183 4	1184 ,	185	1186	1187

EP 1 108 790 A2

					T						<u>.c</u>	in or	e (4-		orotein					
5		ç	9		e A		ne protein		-	4	take prote y	sport proter	ıydroxylas	ine proteir	-binding	ane proteir		ChaA		ane proteii
10		Function	cysteine desulphurase	nicotinate-nucleotide pyrophosphorylase	quinolinate synthetase	DNA hydrolase	hypothetical membrane protein	hypothetical protein	hypothetical protein	lipoate-prote.n ligase	alkylphosphonate uptake protein and C-P lyase activity	transmembrane transport protein or 4-hydroxybenzoale transporter	p-hydroxybenzoate hydroxylase (4-ihydroxybenzoate 3-imonooxygenase)	hypothetical membrane protein	ABC transporter ATP-binding protein	hypothetical membrane protein		Ca2+/H+ antiporter ChaA	hypothetical protein	hypothetical membrane prolein
15		Matched length (a.a.)	376	283	361	235	192	214	108	216	148	420	395	191	532	250		339	236	221
20		Similarity (%)	73.4	689	77.6	6.09	54.7	66.4	74.1	2 09	8.09	64.3	9.89	9.69	47.6	61.6		0.69	57.6	61.1
		Identity (%)	43.9	42.1	49.3	37.0	23.4	36.0	41.7	1 30.1	29.7	28.8	40.8	36.7	24.8	25.6		33.3	28.4	27.6
25	intinued).	gene	faciens ise gene	ercu!osis	A	solor	lurans R1	color	2 MG1655	2 lpIA	2 phnB	da pcaK	uginosa phhy	3 ykoE	Y	8 ykoC		aA	Orsay	аF
30	Table 1 (continued)	Homologous gene	Ruminococcus flavefaciens cysteine desulphurase gene	Mycobacterium tuberculosis	Bacillus subtilis nadA	Streptomyces coelicolor SC5B8.07	Deinococcus radiodurans R1 DR1112	Streptomyces coelicolor SC3A7.08	Escherichia coli K12 MG1655 ybdf	Escherichia coli K12 lpIA	Escherichia coli K12 phnB	Pseudomenas putida peaK	Pseudomonas aeruginosa phhy	Bacillus subtilis 168 ykoE	Escherichia coli yijK	Bacillus subtilis 168 ykoC		Escherichla co'l chaA	Pyrococcus abyssi Orsay PAB1341	Bacillus subtilis ywaF
<i>35</i> 40		db Match	gp:RFAJ3152_2 R	SP.NADC_MYCTU N	pir.E69663 B	7	gp.AE001961_5	gp:SC3A7_8	sp:YBDF_ECOLI	qp:AAA21740 1 E	-	SP PCAK_PSEPU	Sp.PHHY_PSEAE	pir.A69859	ECOLI	88		Sp:CHAA_ECOL!		sp:YWAF_BACSU
40			-	837 sp.N/	IN	642 gp.S(	600 gp.Al	600 gp:S	342 sp:Yl	789 qp:A	<del>                                     </del>	1293 sp.P	1185 sp.P	588 pir.A	1 80	753 pir.G	531	1050 sp.C	708 pir C	723 sp.Y
45		inal ORF (bp)	832 1074		751 118	<del> </del>	<del></del>	-		+-	┼	+	1124835 11	1127009 5	+	╅╌	1129632 5	1136704 1		1131401 7
		Terminal (nl)	1115832	1116908	1117751	1119086	1120804	1120833	1121468	3 1121818		1123534	_!		-	ļ	┺.	<del>  -</del>		1
50		Iritial (nt)	1116905	1117744	1118932	11:9727	1120205	1121432	1121809	1122606		1124826	1126020	1126422		<u> </u>	4702 1129102	1129655		:132:23
		SEQ NC.	4688	4689	4690		4692	4693	4694	2692		4697	4698	4699	_	$\dot{-}$	+-	<u> </u>	<del></del> -	4705
55		SEQ NO.	1188	1189	1190	1191	1192	1193	1194	1105	1195	1197	1198	199	92,	120	.202	1203	1204	1205

			1	- · <del></del>		1	1	т—-	7	_		_		<del>-</del> -		<del></del> -	<del>,</del>			· .		
5		Function	excinuclease ABC subunit A	eroxidase			hypothetical membrane protein	se or thiamin protein			:		118	arsenate reductase (arsenical pump modifier)	hypothetical membrane protein	rotein	rotein	GTP-binding protein (tyrosine phsphorylated protein A)	rotein	rotein		e-4S]
10			excinuclease	thioredoxin peroxidase			hypothetical r	oxidoreductase or thiamin biosynthesis protein					chymotrypsin Bil	arsenate redu modifier)	hypothetical n	hypothetical protein	hypothetical protein	GTP-binding protein (tyre phsphorylated protein A)	hypothetical protein	hypothetical protein		ferredoxin [4Fe-4S]
15		Matched length (a.a.)	946	164			318	282					271	111	340	147	221	614	506	315		103
20		Similarity (%)	58.7	81.7			72.0	49 0					51.3	72.1	62.4	71.4	62.9	76.7	54.9	61.9		91.3
		Identity (%)	35.5	57.3			39.9	34.0					28.8	43.2	23.5	43.5	35.8	46.3	27.9	38.7		78.6
25	Table 1 (continued)	. s gene	philus unrA	uberculosis			edL	elicator A3(2)					ei		aD	berculosis	berculosis	12 typA	berculosis	berculosis		eus fer
<b>30</b>	Table 1	Homologous gene	Thermus thermophilus unrA	Mycobacterium tuberculosis H37Rv tpx			Escherichia coli yedL	Streptomyces coelicator A3(2)					Penaeus vannamei	Escherichia coli	Bacillus subtilis yyaD	Mycobacterium tuberculosis H37Rv Rv1632c	Mycobacterium tuberculosis H37Rv Rv1157c	Escherichia coli K12 typA	Mycobacterium tuberculosis H37Rv Rv1166	Mycobacterium tuberculosis H37Rv Rv1170		Streptomyces grseus fer
<i>35</i> <i>40</i>		db Match	SP. UVRA_THETH	sp:TPX_MYCTU		,,	sp.YEDI_ECOLI	gp:SCF76_2					sp:CTR2_PENVA_F	sp:ARC2_ECOLI	sp:YYAD_BACSU E	pir:F70559	pir.F70555 A	SP:TYPA_ECOLI E	pir.F70874 H	pir.B70875		sp.FER_STRGR S
		ORF (bp)	2340 s	495 s	215	1776	954 s	6 006	365	297	261	387	834 s	345 sı	1200 s	537 p	714 p	1911 sr	1506 pi	iq C78	438	315   sp
45		Terminal (nt)	1132133	1135055	1135691	1135058	1136938	1138859	1139245	1139492	1139617	1139635	1140028	1140501	1142472	1142479	1143026	1146028	1147602	1148461	1148882	1149267
50		initial (nt)	1134472	1134561	1135476	1136833	1137891	1137960	1138880	1139196	1139357	1.40021	1140861	1141245	1141273	1143015	1143739	1144118	1146097	1147592	1148445	1148953
		SEQ NO.	4706	4707	4708	4709	4710	4711	4712	4713	4714	4715	4716	4717	4718	4719	4720	4721	4722	4723	4724	4725
55	المتمسر.	SEQ NO (DNA)	1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1215	1217	1218	1219	1220	1221	1222	1223	1224	1225

EP 1 108 790 A2

5	Function	aspartate aminotransferase				tetrahydrodipicolinate succinylase or succinylation of piperidine-2,6- dicarboxylate		hypothetical protein	dihydropleroate synthase	hypothetical protein	hypothetical protein	antigen TbAAMK, useful in vaccines for prevention or treatment of tuberculosis	mycinamicin-resistance gene	sucrose-6-phosphate hydrolase	ADPglucosestarch(bacterial glycogen) glucosyltransferase	glucose-1-phosphate adenylyltransferase	methyltransferase	RNA polymerase sigma factor (sigma-24); heat shock and oxidative stress	
15	Matched length	397	Š,			229		211	273	245	66	47	286	524	433	400	93	194	
20	Similarity (%)	52.0	37.3			100.0		100.0	0 69	73.1	67.7	91.5	67.8	51.0	51.3	81.8	62.4	57.2	
	Identity (%)	25.0	8.62			100.0		100.0	59.0	45.7	31.3	72.3	39.2	23.5	24.7	61.0	25.8	27.3	
25 (Parcitics)	us gene	744.0 244	Strain Y-M-Z aat			glutamicum D		glutamicum	elicolor A3(2)	prae u17561	Jberculosis	uberculosis	gr seorubida	itosaceus scrB	K12 MG1655	elicolor A3(2)	ycarofaciens	гроЕ	
30	Homologous gene		Bacillus sp. strain			Corynebacterium glutamicum ATCC 13032 dapD		Corynebacterium glutamicum ATCC 13032 orf2	Streptomyces coelicalor A3(2) dhpS	Mycobacterium leprae u17561	Mycobacterium tuberculosis H37Rv Rv1209	Mycobacterium tuberculosis	Micromonospara gr seorubida myrA	Pediococcus pentosaceus scrB	Escherichia coli K12 MG1655 glgA	Streptomyces coelicalor A3(2) glgC	Streptomyces mycarofaciens MdmC	Escherichia coli rpoE	
35	db Match	000	BACSP			gp:CGAJ4934_1				gp:MLU15180_14 N		gsp:W32443	sp:MYRA_MICGR	4 SP.SCRB_PEDPE	<b>—</b>	5 sp. GLGC_STRCO	SP.MDMC_STRMY	sp:RPOE_ECOLI	
40			sp.AAT	İ	2			pir.S60064	gp:SCP8_4	Ť	1 —	<del>                                     </del>	i	4 sp.SC	7 sp.GL	5 sp.GL	<u> </u>		2
	ORF.	3	<u>.</u>	621	1185	891	663	768	R31	729	306	165	864	149	122	121	639	- 63	49,
45	Terminal	(mil)	1150379	1151028	1152370	1152373	1155875	1157669	1158524	1159252	1159572	1159799	1150728	1150738	1162379	1164916	1164974	1166384	1167067
50	Initial	(mr)	149279	150408	1151186	1153263	1155537	1155902	1157694	1158524		1159635	1159865	1162231	1153605	1163702	1165512	1165746	1166576
	SEQ.	<u> </u>	4726	4727	4728	4729	4730	4731	4732	4733	4734	4735	4736	4737	4738	4739	4740	4741	4742
<i>55</i>	SEO NO.		1226	1227	1228	1229	1230	+	.232	1233		1235	1236	1237		1239	1240	1241	1242

5		Function	hypothetical protein	es.	hypothetical protein	hypothetical protein	hypothetical protein			2-oxoglutarate dehydrogenase	ABC transporter or multidrug resistance protein 2 (P-glycoprotein 2)	hypothetical protein	sh.kimate dehydrogenase	para-nitrobenzyl esterase				tetracycline resistance protein	metabolite export pump of letracenomycin C resistance	
15		th ()		ATPase																
		Matched fength (aa)	112	257	154	434	140			1257	1288	240	255	501				409	444	
20		Similarity (%)	73.2	72.0	83.8	77.0	87.1			99.8	60.4	72.1	61.2	64.7				61.4	64.2	
		Identity (%)	45.5	43.6	60.4	49.8	57.9			99.4	28.8	31.7	25.5	35.7				27.1	32.4	
25	tinued)	gene	culosis		culosis	culosis	culosis			amicum	hinese	culosis						poson	scens tcmA	
30	Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv1224	Escherichia coli mrp	Mycobacterlum tuberculosis H37Rv Rv1231c	Mycobacterlum tuberculosis H37Rv Rv1232c	Mycobacterium tuberculosis H37Rv Rv1234			Corynebacterium glutamicum AJ12036 odhA	Cricetulus griseus (Chinese hamster) MDR2	Mycobacterium tuberculosis H37Rv Rv1249c	Escherichia coli aroE	Bacillus subtilis pnbA				Escherichia coli transposon Tn1721 tetA	Streptomyces giaucescens tcmA	
35 40		db Match	pir.C70508	sp:MRP_ECOLI	pir.B70509	pir.C70509	pir.A70952			prf.2306367A	sp:MDR2_CRIGR	pir.H70953	sp:AROE_ECOLI	sp:PNBA_BACSU				sp:TCR1_ECCLI	sp:TCMA_STRGA	
		ORF (bp)	468	1125	579	1290	516	999	594	3771	3741	717	804	1911	651	876	525	1215	1347	705
45		Terminal (nt)	1157577	1167587	1158747	1159321	1171187	1171871	1171869	1172501	-176308	1183121	:180872	183603	184257	1185155	185218	187039	.188389	1190526
50		nitial (nt)	1167110	1168711	1169325	1170610	1170672	1:71206	1:72462	1176271	1180048	1180837	1181675	1181993	4755 1183607	1184280	1185742	4758 1185825	4759 1167043	4760 1189822
		SEQ NO.	4743	4744	4745	4746	4747	4748	4749	4750	4751	4752	4753	4754		4756	4757	4758	4759	
55		SEQ NO.	1243	1244	1245	1246	1247	1248	1249	1250	1251	1252	1253	1254	1255	1256	1257	1258	1259	1260

EP 1 108 790 A2

5 10	Function	5- methyltetrahydropteroyltriglulamate- -homocysteine S-methyltransferase		thiophene biotransformation protein						ABC transporte:	ABC transporter	cytochrome bd-type menaquinol oxidase subunit I!	cytochrome bd-type menaquinol oxidase subunit l	helicase		mutator mutT p:otein ((7,8-dihydro- 8-oxoguanine triphosphatase)(8- oxo-dGTPase)(dGTP pyrophosphohydrolase)		proline-specific permease
15	Matched length (a.a.)	774		444						526	551	333	512	402		86		433
20	Similarity (%)	72.2		79.5						63.5	58.4	93.C	99.0	55.0		656		850
	Identity (%)	45.2		55.2						28.7	29.4	92.0	9.66	26.4		36.9		51.3
25				€B1						55	55	ım ntum)	ım ntum)	55				<b>}</b>
os Table 1 (continued)	Homologous gene	Catharanthus roseus metE		Nocardia asteroides strain KGB1						Escherichia coli K12 MG1655 cydC	Escherichia coli K12 MG1655 cydD	Corynebacterium glutamicum (Brevibacterium lactofermentum) cydB	Corynebacterium glutamicum (Brevibacterium lactofermentum) cydA	Escherichia coli K12 MG1655 yejH		Proteus vulgaris mut T		Salmonella typhimurium proY
40	db Match	pir.S57636		. gsp: Y29930						sp. CYDC_ECOLI	sp:CYDD_ECOLI	gp:AB035066_2	gp.AB035066_1	sp:YEJH_ECOLI		Sp.MUTT_PROVU		sp.PROY_SALTY
	ORF (bp)	2235	455	1398	324	945	792	1647	192	1554	1533	666	1539	2255	342	393	765	1404
45	Terminal (nt)	1188388	119:542	1193807	1194190	1195109	1195125	1197620	1197815	1197990	1199543	1231090	1202094	1203916	1206657	1206831	1208138	1208212
50	Initial (nt)	1190622	1191087	1192410	1193867	1194165	1195916	1195974	1197624	1199543	1201075	1202088	1203632	1206180	1206316	1207223	1237374	1239615
	SEQ NO	<del>+-</del>	4762	4763	4764	4765	4766	4767	4768	4769	4770	4771	4772	4773	4774	4775	4776	4777
55	SEQ NO ONA)	<del></del>	1262	1263	1264	1265	1266	1267	1268	1269	1270	1271	1272	1273	1274	1275	1276	1277

		<del></del>		·							.,							
5	Lo	endent RNA	orotein, tetR		ase	nase			Itor									
10	Function	DEAD box ATP-dependent RNA helicase	bacterial regulatory protein, tetR family	pentachlorophenol 4- monooxygenase	maleylacetate reductase	catechol 1,2-dioxygenase		hypothetica: protein	transcriptional regulator		hypothelical protein	phosphoesterase	hypothetical protein			esterase or lipase		
15	Matched length (a.a.)	643	247	565	354	278		185	878		203	395	915			220		
20	Identity Similarity (%)	74.3	47.4	47.7	72.0	59.4		58.4	55.4		56.2	67.3	59.6			64.6		
	Identity (%)	48.1	24.7	24.5	40.4	30.6		31.9	24.9		29.6	39.2	29.7			37.3		
30 30 Table 1 (continued)	s gene	niae CG43 pendent RNA	'ae	а рсрВ	B13 clcE	aceticus		erculosis	revisiae		color A3(2)	erculosis	erculosis			ig bacterium		
30 Sapple 1 (C	Homologous gene	Klebsiella pneumoniae CG43 DEAD box ATP-dependent RNA helicase deaD	Mycobacterium leprae B1308_C2_181	Sphingomonas flava pcpB	Pseudomonas sp. B13 clcE	Acinetobacter calcoaceticus catA		Mycobacterium tuberculosis H37Rv Rv2972c	Saccharomyces cerevisiae SNF2		Streptomyces coelicolor A3(2) or'Z	Mycobacterium tuberculosis H37Rv Rv1277	Mycobacterium tuberculosis H37Rv Rv1278			Petroleum-degrading bacterium HD-1 hde		
35	£							e2 ⊥				ZI						
40	db Match	sp:DEAD_KLEPN	prf.2323363BT		SDICICE FSESS	sp.CATA_ACICA		pir.A70672	sp.SNF2_YEAST		gp:SCO007731_6	pir.E70755	sp:Y084_MYCTU			gp:AB029896_1		
	ORF (99)	2196	687	1590	1068	885	471	540	3102	1065	858	1173	2628	306	318	774	378	786
45	Terminat (nt)	1212129	1212429	1214858	1215938	1216836	1215904	1217443	1222996	1221841	1223843	1225059	1227693	1227282	1227340	1229636	1229095	1229935
50	Init al (nt)	1209934	1213115	1213269	1214871	1215952	12.7374	12.7982	12:9895	1222905	1222986	1223887	1225066	1227587	1227657	1227863	1228718	1229150
į	SEQ NO (8.8.)	4778	4779		4781	4782	4783	4784	4785	4786	4787	4788	4789	4790	4791	4792	4793	4794
55	SEQ NO. (DNA)	1278	1279	1280	1281	1282	1283	1284	1285	1286	1287	1288	1289	1290	1291	1292	1293	1294

5		Function	short-chain fatty acids transporter	regulatory protein			fumarate (and nitrate) reduction regulatory protein	mercuric transort protein periplasmic component precursor	zinc-transporting ATPase Zn(II)- translocating P-type ATPase	GTP pyrophosphokinase (ATP:GTP 3-pyrophosphotransferase) (ppGpp synthetase I)	tripeptidyl aminopeptidase			homoserine dehydrogenase		-	nitrate reductase gamma chain	nitrate reductase delta chain	nitrate reductase beta chain	hypothetical protein	hypothetical protein	nitrate reductase alpha chain	nitrate extrusion protein
15		Matched length (aa)	122	166			228	18	909	137	601			24			220	175	505	137	83	1271	461
20		Similarity (%)	69.7	56.6			67.9	66.7	9:02	58.4	49.3			98.0			9.39	63.4	83.4	46.0	95.0	73.8	67.9
		identity (%)	37.7	24.7			25.0	33.3	38.0	32.9	26.6			95.0			45.0	30.3	56.6	36.0	36.0	46.9	32.8
25	Table 1 (continued)	ıs gene	licolor	emi recS			12 MG1655 fnr	aciens merP	12 MG1655	ď	Jans tap			glutamicum			arl	arJ	arH	x K1 APE1291	x K1 APE1289	arG	<12 narK
30	Table 1 (	Homologous gene	Streptomyces coelicolor SC1C2.14c atoE	Erwinia chrysanthemi recS			Escherichia coli K12 MG1655 fnr	Shewanella putrefaciens merP	Escherichia coli K12 MG1655 atzn	Vibrio sp. S14 relA	Streptomyces lividans tap			Corynebacterium glutamicum			Bacillus subtilis narl	Bacillus subtilis narJ	Bacillus subtilis narH	Aeropyrum pernix K1 APE1291	Aeropyrum pernix K1	Bacillus subtilis narG	Escherichia coli K12 narK
35				ERWCH E					1				<del>  -</del> 				BACSU		<del>                                     </del>	一		ACSU	1
40		db Match	sp:ATOE_ECOLI	sp.PECS_EF			Sp.FNR_ECOL	sp.MERP_SHEPU	sp ATZN_ECOLI	sp:RELA_VIBSS	gsp:R80504			GSP P61449			sp:NARI_B	sp:NARJ_BACSU	Sp.NARH BACSU	PIR: D72603	PIR 872803		+
		ORF (bp)	537	486	222	519	750	234	1875	630	1581	8	120	108	1260	069	777	732	1593	594	273	+``	1-7
45		Terminal (nt)	1229180	1230480	1230831	1230914	1232479	1232836	1234881	1235612	.236545	.241554	1242156	1243728	.243942	1244843	1245720	1246508	-247199	-250444	↓_	┿	
50		hitial (nt)	1229716	1229995	1230610	1231432	1231730	1232603	1233007	1234983	1238125		1242275	1243521	4807 1245201	1245532	1246496	4810 1247239	4811. 1248791	4812 1249851	4813: 1251545	4814 1252537	1315 4815 1253906
		SEQ NO.	4795	4796	4797	4798	4799	4800	4801	4802	4803	4804	4805	4806	4807	4808	4809		_	÷	_	4814	4815
55		SEQ NO.	1295	1295	1297	1298	1299	1300	1301	1302	1303	1304	1305	1306	1307	1308	1309	1310	1311	1312	1313	1314	1315

					,						<del>,</del>										
5			Ē	thesis cnx1 cofactor cnx1)	otease		ne protein	ne protein	e dinucleotide	nesis protein	hsisi protein denum nzyme)	-CoA ligase					factor 1	idase			ate alpha-N- nsferase
10			Function	molybdopterin biosynthesis cnx1 protein (molybdenum cofactor biosynthesis enzyme cnx1)	extracellular serine protease precurosor		hypothelical membrane protein	hypothetical membrane protein	mo ybdopterin guanine dinucleotide synthase	mo ybdoptein biosynthesis protein	mo ybdopterin biosynthsisi protein Moybdenume (mosybdenum cofastor biosythesis enzyme)	edium-chain fatty acid-CoA ligase	Rho factor				peptide chain release factor	protoporphyrinogen oxidase		hypothetical protein	undecaprenyl-phosphate alpha-N- acetylglucosaminyltransferase
15			Matched length (a.a.)	157	738		334	472	178	366	354	572	753				363	280		215	322
20			Similarity (%)	65.0	45.9		62.6	60.2	52.3	58.2	73.7	65.7	73.8				71.9	57.9		86.0	58.4
			Identity (%)	32.5	21.1		30.8	31.6	27.5	32.8	51.4	36.7	50.7				41.9	31.1		62.3	31.1
<b>25</b>		Table 1 (continued)	us gene	na CV cnx1	ins strain IFO.		berculosis	berculosis	ida mobA	berculosis noeA	2xub en	ovorans	s rha				12 RF-1	12		oerculosis	12 rfe
30		Table 1 (	Homologous gene	Arabidopsis thaliana CV cnx1	Serratia marcescens strain IFO- 3046 prtS		Mycobacterium tuberculosis H37Rv Rv1841c	Mycobacterium tuberculosis H37Rv Rv1842c	Pseudomonas putida mobA	Mycobacterium tuberculosis H37Rv Rv0438c moeA	Arabidopsis !haliana cnx2	Pseudomonas oleovorans	Micrococcus luteus rho	-			Escherichia coli K12 RF-1	Escherich a coli K12		Mycobacterium tuberculosis H37Rv Rv1301	Escherich a coli K12 rfe
<i>35</i>			db Match	Sp:CNX1_ARATH	SP.PRTS_SERWA		sp:Y0D3_MYCTU	Sp. Y0D2_MYCTU	gp:PPU242952_2	Sp:MOEA_ECOLI	sp.CNX2_ARATH //	SP:ALKK_PSEOL F	Sp.RHO_MICLU				sp:RF1_ECOLI	Sp:HEMK_ECOLI E		sp:YD01_MYCTU	sp.RFE_ECOLI
			04년 (bp)	489 s	s 998:	684	1008 s	1401 s	551 g	1209 s	1:31	1725 s	2286 sı	603	969	1023	1074 s <sub>l</sub>	837 SI	774	648 s <sub>l</sub>	1146 SJ
45			Terminal (nt)	1254634	1254737	1257750	1255851	1257865	1259429	1259993	1261688	1262886	1267427	1266267	1265611	1265427	1268503	1269343	1268267	1270043	1271192
50			Initial (nt)	1254146	1256602	1257067	1257858	1259265	1259989	1261201	1262818	1264610	1265142	1265665	1266306	1266449	1267430	1268507	1269040	1269396	1270347
	•		SEQ NO. (a a.)	4616	4617	4618	4619	4620	4621	4622	4623	4824	4£25	4826	4627	4628	4629	4630	4631	4632	4633
55			SEQ NO (DNA)	1316	1317	1318	1319	1320	1321	1322	1323	1324	1325	1326	1327	1328		1330	1331	1332	1333

															$\overline{}$			
5		Function		nis	ain a (protein 6)	ATP synthase lipid- ATP synthase C	H+-transporting ATP synthase chain b	H+-transporting ATP synthase delta chain	H+-transporting ATP synthase alpha chain	ATP synthase	H+-Iransporting ATP synthase beta chain	ATP synthase	ein	ein	P-binding protein	ein	in	
10		Fun		hypothetical protein	ATP synthase chain a (protein 6)	H+-transporting ATP synthase birding protein. ATP synthase chane	H+-transporting A b	H+-transporting A chain	H+-transporting A chain	H+-transporting A gamma chain	H+-transporting A chain	H+-transporting A epsiton chain	hypothetical protein	hypothetical protein	putative ATP/GTP-binding protein	hypothetical protein	hypothetical protein	thioredoxin
15		Matched length (a.a.)		80	245	7.1	151	274	516	320	483	122	132	230	92	134	101	301
20	···	Similarity (%)		0.66	56.7	85.9	6.99	67.2	88.4	76.6	100.0	73.0	67.4	85.7	26.0	68.7	79.2	71.4
		Identity (%)		0.86	24.1	54.9	27.8	34.3	6.99	46.3	8.66	41.0	38.6	70.0	45.0	35.8	545	37.9
25	Table 1 (continued)	ons gene		ı glutamicum	K12 alpB	idans atpL	idans atpF	idans atpD	idans atpA	idans atpG	n glutamicum	idans atpE	uberculosis	uberculosis	elicolor A3(2)	⁄qjC	uberculosis	uberculosis
<b>30</b>	Tahle 1	Homologous gene		Corynebacterium glutamicum atpl	Escherichia coli 1	Streptomyces lividans atpL	Streptomyces lividans atpF	Streptomyces lividans atpD	Streptomyces lividans atpA	Streptomyces lividans atpG	Corynebacterium glutamicum AS019 atpB	Streptomyces lividans atpE	Mycobacterium tuberculosis H37Rv Rv1312	Mycobacterium tuberculosis H37Rv Rv1321	Streptomyces coelicolor A3(2)	Bacillus subtilis yajC	Mycobacterium tuberculosis H37Rv Rv1898	Mycobacterium tuberculosis H37Rv Rv1324
<i>35</i>		db Match		GPU:AB046112_1	sp:ATP6_ECOLI	sp.ATPL_STRLI	SP:ATPF_STRLI	SP.ATPD_STRLI	sp:ATPA_STRLI	SP.ATPG_STRLI	sp:ATPB_CORGL	sp:ATPE_STRLI	sp:Y02W_MYCTU	sp.Y036_MYCTU	GP:SC26G5_35	sp:YQJC_BACSU	sp:YC20_MYCTU	sp:YD24_MYCTU
		ORF (bp)	486	249 G	810 sp	ಲ್ಲ	564 sp	613 sp	1674 sp	975 sp	1449 sp	372 sp	471 SF	s 069	285 G	453 sp	312 sp	921 sp
45		Terminal (nt)	1271698	1272119	1273149	1273525	1274122	1274943	1276648	1277682	1279136	1279522	1280240	1280959	1281251	1281262	1282105	1283114
50		(nitial	1271213	1271871	1272340		1273559	1274131	1274975	1276708	1277688	1279151	1279770	1280270	1280967	1281714	1281794	1282194
		SEQ NO (a a.)	4834	4835	4836	<del></del>	4838	4839	4840	4841	4842	4843	4844	4845	4846	4847	4848	4849
<i>55</i>		SEQ NO.	1334	1335	1336	1337	1338	1339	1340	1341	1342	1343	1344	1345	1346	1347	1348	1349

·5
10
15
20
25
30
35
40
45
50

Table 1 (continued)	Function	FMNH2-dependent aliphatic sulfonate monooxygenase	alphatic sulfonates transport permease protein	alphatic sulfonates transport permease prolein	sulfonate binding protein precursor	1,4-alpha-glucan branching enzyme (glycogen branching enzyme)	alpha-amylase		ferric enterobactin transport ATP- binding protein or ABC transport ATP-binding protein	hypothetical protein	hypothetical protein		electron transfer flavoprotein beta- subunil	electron transfer flavoprotein alpha subunit for various dehydrogenases		nitrogenase cofactor sythesis protein		hypothetical protein
	Matched ength (a.a.)	366	240	228	311	710	467		211	260	367		244	335		375		397
	Similarity (%)	74.3	75.8	72.8	62.1	72.7	50.5		87.6	68.5	70.0		64.8	61.8		67.7		55.7
	Identity (%)	50.3	40.8	50.4	35.1	46.1	22.9		31.8	39.6	43.1		31.2	33.1		35.2		29.5
	Homologous gene	Escherichia coli K12 ssuD	Escherichia coli K12 ssuC	Escherichia coli K12 ssuB	Escherichia coli K12 ssuA	Mycobacterum tuberculosis H37Rv Rv1326c glgB	Dictyoglomus thermophilum amyC		Escherichia coli K12 fepC	Mycobacterium tuberculosis H37Rv Rv3040c	Mycobacterium tuberculosis H37Rv Rv3037c		Rhizobium meliloti fixA	Rhizobium meliloti fixB		Azotobacter vinelandii nifS		Rhizobium sp NGR234 plasmid pNGR234a y4mE
	db Match	3.gp ECO237695_3	sp:SSUC_ECOL!	sp:SSUB_ECOU	sp.SSUA_ECOLI	so GLGB_ECOL!	sp.AMY3_D:CTH		sp.FEPC_ECOLI	pir C70860	o r H70859		SP.FIXA_RHIME	sp:FIXB_RHIME		sp:NIFS_AZOVI		SP Y4ME_RHISN
	ORF (ba)	1143	758	729	957	2193	1494	348	879	804	1056	612	786	951	615	1128	312	1146
:	Terminal (nt)	.284466	1285284	1286030	1286999	:287281	1289514	1291373	1292577	1294025	1295206	:294436	1296220	1297203	1297093	1298339	1298342	:299000
	Initial (nt)	1283324	1284517	1295302	1286043	1289473	1291307	1291026	1291599	1293222	1294151	1295047	1295435	1296253	4863 1296479	4964 1297212	1298553	4366 1300:45
į	SEQ NO. (a.3.)	4850	4851	4852	4953	4854	4855	4856	4857	4858	4959	4860	4861	4952	4863	4364	4955	4366
1	SEQ NO.	1350	1351	1352	1353	1354	1355	1356	1357	1358	1359	1360	1361	1362	1363	1364	1365	1366

5		Function	transcriptional regulator	acety!transferase				IRNA (5-methylaminomethyl-2- thiouridylate)-methyltransferase		hypothetical protein	tetracenomycin C resistance and export protin		DNA ligase (polydeoxyribonucleotide synthase [NAD+]	hypothetical protein	glutamyl-tRNA(Gln) amidotransferase subunit C	glutamyl-tRNA(Gln) amidotransferase subunit A	vibriobactin utilization protein / iron- chelator utilization protein	hypothetical membrane protein	pyrophosphatefructose 6- iphosphate 1-phosphotransrefase
15		Natched length (a.a.)	59	181				361		332	200		677	220	97	484	263	96	358
20		Similarity (%)	76.3	55.3				6.09		66.0	65.8		70.6	70.9	64.0	83.0	54.0	79.2	77.9
		Identity (%)	47.5	34.6				61.8		33.7	30.2		42.6	40.0	53.0	74.C	28.1	46.5	54.E
30	Table 1 (continued)	Hamologaus gene	Rhizobium sp. NGR234 plasmid pNGR234a Y4mF	Escherichia coli K12 MG1655 yhbS				Mycobacterium tuberculosis H37Rv Rv3024c		Mycobacterium tuberculosis H37Rv Rv3015c	Streptomyces glaucescens tcmA		Rhodothermus marinus dn:J	Mycobacterium tuberculosis H37Rv Rv3013	Streptomyces coelicolor A3(2) gatC	Mycobacterium tuberculosis H37Rv gatA	Vibrio vulnificus viuB	Streptomyces coelico.or A3(2) SCE6.24	Amycolatopsis methanolica pfp
35				i	-			My H3		H W			1	E M	<b></b> -	T	_	ည်း လ	1
<b>40</b>		db Match	Sp.Y4MF_RHISN	sp:YHBS_ECOLI				pir:C70858		pir:870857	sp:TCMA_STRGA		sp:DNLJ_RHOMR	pir.H70856	sp.GATC_STRCO	sp.GATA_MYCTU	UVBIV_BUIV qs	gp:SCE6_24	SP PFP_AMYME
		ORF (bp)	225	504	942	1149	396	1095	654	066	1461	735	· · · <del></del>	663	297	1491	849	306	1071
45		Terminal (1;)	1300145	1301055	1300988		1303694	1304923	1303883	1305921	1305924	1307462	1310369	1310435	1311616	1313115	1314118	1314475	1316083
50		Initial (nt)	4867 1300369	1300552 1301055	1301929	1303123 1301975	1303299	4872 1303829	4873:1304536	1304932	4875 1307384	1308196	1377   4877   1308330	1311097	1311320	4880 1311625	488: 1313270	1314775	13150*3
		SEQ NO (a.a.)	4867	4868	4869	4870	4871	4872	4873	4874	4875	4876	4877	4878	1379 4879	4880	488	4882	4883
55		SEO NO (DNA)	1367	1368	1369	1370	1371	1372	1373	1374	1375	1376	1377	1378	1379	1380	1381	1382	1383

				- ·· ·		<del>,</del> - · ·-		<del></del>			۲.	,			<del></del>				
5				nylase ontrol protein)	pinding protein	nsport protein	ding protein	sport protein		ng lipoprotein	d transporter	otransferase B	ent NADH			e protein		Itase	
10		Function		glucose-resistance amylase regulator (catabolite control protein)	ripose transport ATP-binding protein	high affinity ribose transport protein	periplasmic ribose-binding protein	high affinity ribose transport prote:n	hypothetical protein	iron-siderophore binding lipoprotein	Na-dependent bile acid transporter	RNA-dependent amidotransferase B	putative F420-dependent NADH reductase	hypo:hetical protein	hypothetical protein	hypothetica membrane protein		dihydroxy-acid dehydratase	nypothetical protein
15		Matched length	2	328	499	329	305	139	200	354	268	485	172	317	234	325		513	105
20		Similarity (%)		31.4	76.2	76.9	7.77	68.4	58.0	60.2	61.9	71.8	61.1	6.99	62.4	52.6	<u>-</u>	99.4	68.6
		Identily (%)		31.4	44.7	45.6	45.9	41.7	31.0	31.4	35.8	43.1	32.6	39.8	39.3	27.4		99.2	33.3
30 35	Table 1 (continued)	Homologous gene		Bacillus megaterium ccpA	Escherichia coli K12 rbsA	Escherichia coli K12 MG1655 rbsC	Escherichia coli K12 MG1655 rbsB	Escherichia coli K12 MG1655 rbsD	Saccharomyces cerevisiae YIR042c	Streptomyces coelicolor SCF34.13c	Rattus norvegicus (Rat) NTC!	Staphylococcus aureus WHU 29 ratB	Methanococcus jannaschii MJ1501 f4re	Escherichia coli K12 yajG	Mycobacter um tuberculosis H37Rv Rv2972c	Mycobacterium tuberculosis H37Rv Rv3005c		Corynebacterium glutamicum ATCC 13032 itvD	Mycobacterium tuberculos s H37Rv Rv3004
40		db Match		sp:CCPA_BACME	sp.RBSA_ECO:	sp:RBSC_ECOLI	sp:RBSB_ECOLI	sp:RBSD_ECOL:	sp:YIW2_YEAST	gp:SCF34_13	S2 NTC _RAT	gsp W61467	sp.F4RE_METJA	sp:YQJG_ECOLI	pir.A70672	pr:H70855		gp:AJ012293_1	pir:G70855
		ORF (tp)	630	1107	1572	972	942	369	929	1014	1005	.479	672	1077	774	1056	237	1839	564
45		Terminal (nt)	1315325	1317444	1319005	1319976	1320942	1321320	1322111	1323406	1324537	1326256	1327049	1329891	1331875	1333008	1333188	1333442	1335412
50		fnitial (nt)	1315954	1316338	1317434	1319005	1320001	1320952	1321476	1322393	1323533	1324778	1326379	1330967	331102	1331953	1333424	:335280	1335975
		SEQ NC. (a a)	4884	4885	4886	4887	4888	4889	4890	4891	7687	4893	4834	4835	4896	4997	4898	4899	4900
55		SEQ NO (DINA)	1384		1386	1387	1388	1389	1390		1392	1393		1395	1396 4	1397	1398	1399 4	400 4

EP 1 108 790 A2

5	ion	ane protein			P-binding polein	n transport ATP.	rotein			tide dimerase	m resistance					ate	rich protein				
10	Function	hypothetical membrane protein	hypothetical protein		nitrate transport ATP-binding polein	mal:ose/maltodextrin transport ATP- binding protein	nitrate transporter protein			actinorhocin polyketide dimerase	cobalt-zinc-cadimium resistance protein			hypothetical protein		D-3-phosphoglycerate dehydrogenase	hypothetica! serine-rich protein			hypothetical protein	
15	Matched length (a.a.)	62	99		167	87	324			142	304			642		530	105			620	
20	Similarity (%)	100.0	55.0		80.9	78.2	56.8			73.2	72.7			53.7		100.0	52.0			63.1	
	Identity (%)	100.0	45.0		50.9	46.0	28.1			39.4	39.1			22.9		8.66	29.0			32.9	
25 (panuj	eue	amicum	v		무	es is) malK	occ 7120			lor	CD			schii		n serA	s ротbе			tus strain	
8 Table 1 (continued)	Homologous gene	Corynebacterium glutamicum ATCC 13032 yilV	Sulfolobus solfataricus		Synechococcus sp. ndD	Enterobacter aerogenes (Aerobacter aerogenes) malK	Anabaena sp. strain PCC 7120 nrtA			Streptomyces coelicolor	Ralstonia eutropha czcD			Methanococcus jannaschii	-	Brevibacterium flavum serA	Sch zosaccharomyces pombe SPAC11G7 01			Rhodobacler capsulatus strain SB1003	
40	db Match		GP:SSU18930_26		SP NRTD_SYNP7	SP MALK_ENTAE	sp NRTA_ANASP		i	sp DIM6_STRCO	sp.czcD_ALCEU			sp:Y686_METJA		gsp:Y22646	SP:YEN1_SCHPO		-	pır. T03476	
	ORF (bp)	1473.5	231 G	909	498 s	267	882   s	447	369	486 s	954 's	153	069	1815 s	1743	1590 g	327 S	867	1062		402
45	Terminal (nt)	1336055	1338379	1342677	134 ' 960	1342461	1342794	1344464	1344808	1345420	1346439	1345335	1345642	1348272	1350076	1352444	1351727	:353451	1354540	1357554	1356853
50	Initial (nt)	1337557	1338639	1342072	1342457	1342727	1343675	1344018	4938 1344443	1344935	4910 1345485	1345487	1346331	1346458	1348334	1350855	1352053	1352585	1355601	1355589	1355452
	SEQ NO (a.a.)	4901	4932	4933	4604	4935	4909	4937		4939	•	4911	4912	4913	4914	4915	4916	4917	4918	4919	4920
55	SEQ NO ONA)	1401	1402	1403	1404	1405	1406	1407	1408	1409	1410	14:1	14:2	1413	1414	1415	14.6	1417	14:8	1419	1420

5			catabolism ase [includes: ene-1,7-dioate srase]; 5- nex-3-ene-1,7- opet	3-0-	a <sub>v</sub>	ase														rotein
10	Function		homoprotocatechiuate catabolism bifunctional isomerase/decarboxylase [includes: 2-hydroxyhepta-2, 4-diene-1,7-dioate isomerase(hhdd isomerase), 5-tranboxymethyl-2-oxo-hex-3-ene-1,7-dioate decarboxylase(opet decarboxylase)	methyltransferase or 3- deme:hylubiquinone-9 3-O- methyltransferase	isochorismate synthase	glutamyl-tRNA synthetase	transcriptional regulator													thiam n biosynthesis protein
	Matched length (a.a.)		228	192	371	485	67													599
20	Similarity (%)		59.2	55.7	70.4	69.7	90.0			-										81.0
. «-	Identity (%)		33.3	23.4	38.0	37.3	77.0				·									65.1
75 Sable 1 (continued)	Hcmologous gene		О прсЕ	(12	hbc	¥	elicolor A3(2)													niA or thiC
35 Table 1	Hcmolog		Escher chia coli C hpcE	Escherichia coli K12	Bacillus subtillis dhbC	Bacillus subtilis gitX	Streptomyces caelicolar A3(2)													Bacilus subtilis thiA or thiC
40	db Match		so:HPCE_ECOLI	sp.'JBIG_ECOLI	8 sp DHBC_BACSU	8 sp:SYE_BACSU	gp.SCJ33_10													sp:THIC_BACSU
	ORF (bp)	654	804	618	1128	1488	213	516	522	342	621	303	180	330	213	183	318	1152	324	176
45	Terminal (nt)	1358210	1359062	1359669	1360168	1362848	1362926	1363142	1363732	1365256	1364340	1364878	1365217	1366137	1367505	1367888	1368395	1369551	1369874	1369877
50	Initial (rt)	1357557	4922 1358255	4923 1359052	1361295	1361361	1363138	1363657	1364253	4929 1364915 1365256	1364960	1365180	1365396	1433 4933 1365808	4934, 1367293	4935 1368070	1368078	1368400	1369551	1371637
,	SEQ NO (a.a)	1921	4922	4923	4924	4925	4926	4927	4928	4929	4930	4931	4932	4933	4934	4935		4937		4939
55	SEO NO (DVA)	1421	1422		1424	1425	1426	1427		1429	1430	1431	1432	1433	1434	1435	1436	1437	1438 4938	:439

5		Function			lipoprotein		glycogen phosphorylase			hypothetical protein	hypothetical membrane protein		guanosine 3,5-bis(diphosphate) 3'- pyrophosphatase	acetate repressor protein	3-isopropylmalate dehydratase large subunit	3-isopropylmalate dehydratase small subunit		mutator mutT protein ((7,8-dihydro- 8-oxoguanine-triphosphatase)(8- oxo-dGTPase)(dGTP pyrophosphohydrolase)		NAD(P)H-dependent dihydroxyacetone phosphate reductase	D-alanine-D-alanine ligase
15		Matched length (a.a.)			44		797			299	256		178	257	473	195		294		331	374
20		Similar ty (%)			74.0		74.0			52.8	64.8		60.1	60.7	87.5	89.2		71.4		72.2	67.4
		Identity (%)			61.0		44.2			25.4	25.4		29.8	26.1	68.1	67.7		45.9		45.0	40.4
25	ned)	au .									hii Y441		10	~	eticus			losis			31655
30 35	Table 1 (continued)	Hamologous gene			Chlamydia trachomatis		Rattus norvegicus (Rat)			Bacillus subtilis yrkH	Methanoccccus jannaschii Y441		Escherichia coli K12 spoT	Escherichia coli K12 iclR	Actinoplanes teichomyceticus leu2	Salmonella typhimurium	,	Mycobacterium tuberculosis H37Rv MLCB637.35c		Bacillus subtilis gpdA	Escherichia coli K12 MG1655 dcIA
40		db Match			GSP: Y37857		sp.PHS1_RAT			sp.YRKH_BACSU	sp: V441_METJA		sp:SPOT_ECOLI	sp ICLR_ECOLI	sp:LEU2_ACTTI	sp:LEUD_SALTY		gp:MLCB637_35		sp.GPDA_BACSU	sp.DDLA_ECOL!
		ORF (bp)	348	53:	132	936	2427	183	156	1407	750	477	564	705	1443	591	318	954	156	966	1080
45		Termina (nt)	1371979	1373131	1373929	1375491	1273350	1375805	1375933	1376149	1377666	137846E	1379566	1379555	1381882	1382492	1382502	1382845	1384085	1385125	1386232
50		Initial (nt)	1372326	1372601	1373798	1374556	1375776	1375987	1376088	1377555	13784:5	1378942	1379003	1380259	1380440	1381902	1382819	1383798	1383930	1384130	1385153
		SEO NO.	4940	4541	4942	4943	4944	4945	4946	4947	4948	4949	4950	4951		4953	4954	4955	4956	4957	4958
55		SEQ NO.	. 1440	1441	1442	1443	1444	1445	1445	1447	1448	1449	1450	1451		1453	1454	1455	1456	1457	1458

5				lase	e precursor		helicase	to be useful and	protein		re biosynthesis		s predicted to vaccines and	glutamine ABC nding protein	tein	lein precursor		e protein		
10		Function		thiamin-phosphate kinase	uracil-DNA glycosylase precursor	hypothetical protein	ATP-dependent DNA helicase	polypeptides predicted to be useful antigens for vaccines and diagnostics	biotin carboxyl carrier protein	methylase	lipopolysaccharide core biosynthesis protein		Neisserial polypeptides predicted to be useful antigens for vaccines and diagnostics	ABC transporter or glutamine AB transporter, ATP-binding protein	nopaline transport protein	glutamine-binding protein precursor		hypothetical membrane protein		phage integrase
15		Matched iength (a a)		335 #	245 U	568 h	693 A	108 g e ib	67 bi	167 m	155 lip	·   	65	252 A	220 nc	234 gl	-	322 h		223 pt
20		Similarity (%)		57.6	59.6	56.3	0.09	48.0	67.2	63.5	7.8.7		74.0	78.6	75.0	59.0		60.3		52.5
		Identity (%)		32.2	38.8	23.1	35.4	31.0	38.8	37.1	42.6		67.0	56.4	32.7	27.4		28.6		26.9
<i>25</i> <i>30</i>	Table 1 (continued)	Homologous gene		Escherichia coli K12 thiL	culus ung	Mycoplasma genita'ium (SGC3) MG369	Escherichia coli K12 recG	Neisseria meningitidis	Propionibacterium freudenreichii subsp. Shermanii	Escherichia coli K12 yhhF	Escherichia coli K12 MG1655 kdtB		Neisseria gonorrhoeae	Bacillus stearothermophilus	Agrobacterium tumefaciens nocM	Escherichia coli K12 MG1655 ginH		Methanobacterium thermoautotrophicum MTH465		Bacteriophage L54a vinT
35	<b>F</b>	Ĭ		Escherich	Mus musculus ung	Mycoplas MG369	Escherich	Neisseria	Propionibacterium subsp. Shermanii	Escherich	Escherich kdtB		Neisseria	Bacillus si glnQ	Agrobacte nocM	Escherich glnH		Methanobacterium thermoautotrophics		Bacteriopl
40		db Match		Sp: THIL_ECOLI	sp.UNG_MOUSE	sp:Y369_MYCGE	sp:RECG_ECOL!	GSP:Y75303	sp:BCCP_PROFR	sp:YHHF_ECOLI	sp:KDTB_ECCLI		GSP:Y75358	sp.GLNQ_BACST	sp:NOCM_AGRT5	sp:GLNH_ECOLI		pir:H69160		sp:VINT_BPL54
	į	(pp)	978	993	762	1581	2121	324	213	582	480	1080	204	750	843	861	807	978	408	756
45		Terminał (nt)	1386293	1388324	1389073	1390788	1392916	1391638	1393151	1393735	1394221	1395933	1395097	1394800	1395568	1396561	1398468	1398557	1401333	1400185
50		In tial (nt)	1387270	1387332	1388312	1389208	1390796	1391951 1391638	1392939	1393154	1393742	1394854	1394894	1395549	1396410	1397421	1397662	1399534	4975 1400926	1476 4976 1403943
		SEO NO (a.a.)	4959	4960	496.	4962	4963	4964	4965	4966	4967	4968	4969	4970	4971	4972	4973	4974		4976
55		SEQ NO.	:459	1460	1461	1462	1463	1464	1465	1466	1467	1468	1469	1470	1471	1472	1473	1474	1475	1476

		Γ			_	[	-			Г			<u> </u>		 			Γ				Ī	$\Gamma \gamma$
5							related)										į			otein		enase	
10	Function						insertion element (IS3 related)		hypothetical protein										DNA polymerase I	cephamycin export protein	DNA-binding protein	morphine-6-dehydrogenase	
15	Matched length (a.a.)						56		37		<u>:</u> 								968	456	283	284	
20	Similarity (%)						96.2		97.0										80.8	87.8	65.4	76.1	
	Identity (%)	Ŀ		<u> </u>			88.5		89.0										56.3	33.8	41.3	46.5	
25 (panuituo	gene						utamicum		utamicum										rculosis	ndurans	olor A3(2)	а тогА	
Table 1 (continued)	Homologous gene						Corynebacterium glutamicum orf2		Corynebacterium glutamicum					:			I)		Mycobacterium tuberculosis polA	Streptomyces lactamdurans cmcT	Streptomyces coelicolor A3(2) SCJ9A. 15c	Pseudomonas putida morA	
<i>35</i>	db Match						pir.S60890		PIR:S60890										sp:DPO1_MYCT:J	SP. CMCT_NOCLA	gp:SCJ9A_15	sp:MORA_PSEPU	
	CRF (bp)	744	432	507	864	219	192 p	855	111	369	315	321	375	948	306	564	222	291	2715 s	1422 5	606	873 s	159
45	Terminal (nt)	1402076	1402703	1402368	1403991	1404215	1404694	1405320	1406999	.407167	:407559	:408703	1409428	1410064	1411119	1411437	1412572	1412626	1416459	1416462	1418870	1419748	1419878
50	In tial (nt)	4977 - 1401333	4978 . 1402272	1402874	1403128	4981 1403997	1404885	1406174	1407109	1407535	:407873	.409023	1409802	1411011	1411424	1412000	1412351	1412916	1413745	1417883	1417962	1418876	1420036
بيمس	SEQ NO. (a.a.)	4977		4979	4980	4981	4982	1983	4984	4985	4986	4987	4988	4989	4990	4991	4992	4993	4994	4995	4996	4997	4998
55	SEO NO.	1477	1478	1479	1480	1481	1482	1483	1484	1485	1486	.487	1488	:483	1490	1491	1492	1493	1494	1495	1496	1497	1498

5	Function	al protein	30S ribosomal protein S1		al protein					inosine-uridine preferring nucleoside hypolase (purine nucleosidase)	aniseptic resistance protein	936	criplic asc operon repressor, ranscription regulator		ise ABC subunit B	al protein	al protein	al protein		al protein	al protein	
		hypothetical protein	30S ribosc		hypothetical protein					inosine-uri hypolase (	aniseptic	ribose kinase	criptic asc ranscriptio		excinuclease ABC	hypothetical protein	hypothetical protein	hypothetical protein		hypothetical protein	hypothetical protein	hydrolase
15	Matched length (a.a.)	163	451		195					310	517	293	337		671	152	121	279		939	150	214
20	Similarity (%)	58.3	71.4		93.9					810	53.8	9.79	9.59		83.3	59.2	80.2	177.1		47.2	0.89	58.4
	Identity (%)	31.9	39.5		80.5					61.9	23.6	35.5	30.0		57.4	33.6	38.8	53.8		23.2	32.7	30.4
onlinued)	s gene	color	2 rpsA		ofermentum					iunH	reus	2 rbsK	2 ascG		umoniae /rB	naschii	2 ytfH	2 ytG		St	icolor A3(2)	2 ycbL
S Table 1 (continued)	Homologous gene	Streptomyces coelicolor SCH5.13 yafE	Escherichia coli K12 rpsA		Brevibacterium lactofermentum ATCC 13859 yacE					Crithidia fasciculata iunH	Staphylococcus aureus	Escherichia coli K12 rbsK	Escherichia coli K12 ascG		Streptococcus pneumoniae plasmid pSB470 uvrB	Methanococcus jannaschii MJ0531	Escherichia coli K12 ytfH	Escherichia coli K12 ytfG		Bacillus subtilis yvgS	Streptomyces coelicolor A3(2) SC9H11.26c	Escher chia coli K12 ycbL
<i>35</i>	db Match	Sp YAFE_ECOLI	sp.RS1_ECOLI		sp:YACE_BRELA					sp:IUNH_CRIFA	1449 sp. QACA_STAAU	Sp.RBSK_ECOLI	sp.ASCG_ECO_I		97 sp.UVRB_STRPN	sp:Y531_METJA	sp:YTFH_ECOLI	sp.YTFG_ECOLI		pir:H7004C	gp:SC9H11_26	sp:YCBL_ECOLI
	ORF (bp)	654	1458	1476	900	1098	585	246	957	936	1449	921	1038	798	2097	441	381	978	, 684	2349	9:2	900
45	Terminal (nt)	1420071	1422556	142.096	1425878	1427354	1427376	-427804	1423246	1428224	1429194	1430659	1431575	1433547	1436201	1436775	-436869	1438201	:440026	1438212	:440675	:441793
50	Initial (nt)	1420724	1421099	142257:	1425279	1426257	1427957	1428049	5005 1428290	5007 1429159	1430642	1431579	:432612	1511 5011 1432750	5012 :434105	1436335	1437249	1515 5015 1437356	1516 5016 1439343	1440560	1518 5018 1441586	1442392
	SEQ NO (a.a.)	1499 4939	1500 5033	5031	1502 , 5032	1503 5003	15034	5005	5005	2002	5008	5009	1510 5010	5011	·	1513 5013	1514 5014	5015	5016	1517 5017	5018	5019
55	SEQ NC DNA	1499	1500	1501	1502	1503	1504	1505	1506	1507	1508	1509	1510	1511	1512	1513	1514	1515	1516	1517	1518	1519

		_						,								_			
5	Function	excinuclease ABC subunit A	hypothetical protein 1246 (uvrA region)	hypothetical protein 1245 (uvrA region)			translation initiation factor IF-3	50S ribosomal protein L35	50S ribosomal protein L20			sn-glycerol-3-phosphate transport system permease protein	sn-glycerol-3-phosphate transport system prolein	sn-glycerol-3-phosphate transport system permease proein	sn-glycerol-3-phasphate transport ATP-binding protein	hypothetical protein	glycerophosphoryl diester phosphodiesterase	tRNA(guanosine-2-0-)- methlytransferase	phenylalanyl-tRNA synthetase alpha chain
15		excin	hypothe region)	hypothe region)			transl	50S ri	50S ri			syster syster	sn-gly syster	sn-gly syster	sn-gly ATP-t	hypot	glycer	tRNA meth	pheny chain
	Matched length (a.a.)	952	100	142			179	09	117			292	270	436	393	74	244	153	
20	Similarity (%)	90.6	97.0	47.0			78.2	76.7	92.7			71.6	70.4	57.6	71.3	56.0	50.0	71.2	
·	Identity (%)	56.2	40.0	31.0			52.5	41.7	75.0			33.2	33.3	26.6	44.0	47.0	26.2	34.0	·
25 D						-	ji O		,			655	655	655	655	0042		655	
S S Table 1 (continued)	Homologous gene	Escherichia coli K12 uvrA	Micrococcus Iuteus	Micrococcus luteus			Rhodobacter sphaeroides infC	Mycoplasma fermentans	Pseudomonas syringae pv. syringae			Escherichia coli K12 MG1655 ugpA	Escherichia coli K12 MG1655 upgE	Escherichia coli K12 VIG1655 ugpB	Escherichia coli K12 MG1655 ugpC	Aeropyrum pernix K1 APE0042	Bacillus subtilis glpQ	Escherichia coli K12 MG1655 trmH	Bacillus subtilis 168 syfA
<i>35</i>	db Match	sp.JVRA_ECOLI	PIR.JQ0406	PIR.JQ0406			Sp.IF3_RHOSH	SP RL35 WYCFE	sp.RL20_PSESY	. —		sp:UGPA_ECOLI	sp:UGPE_ECOLI	sp.ugpa_Ecoli	sp:UGPC_ECULI	PIR:E72756	sp.GLPQ_BACSU [	SP.TRMH_ECOLI	sp:SYFA_BACSU
	78. 00	47	06 PIR	450 PIR.	17	24	67 Sp.16		81 sp.R	22			34 sp:U	14	24	249 PIR	sp.G	594 sp.T	8
45	0=	138	<u>۳</u>	<del>i</del>	7	23 2124	5	81 192	<u>س</u>	80	92 567	20 903	60	13	12	$\vdash$			<u> </u>
	Terminal (nt)	1445333	14438	1444944	1446874	1445323	1448358	1448581	1449025	1449119	1450692	1451820	1452653	1454071	1455338	1454102	1455350	1456948	14580
50	fnitial (nt)	1442487	1444115 1443810	1445393	1446159	1447446	1447792	1448390	5027 1448645	1449940	1450125	1450918	5031 1451820	1452758	1454115	1454350	1456036	5036 1456355	5037 1457047 1458066
	SEO NO.	5020	5021	5022	5023	5024	5025	5026	5027	502B	5028	5030	5031	5032	5033	5034	5035		
55	SEO NO (SNA)	1520	1521	. 522	.523	.524	.525	.525	1527	.528	.529	.530	.531	.532	.533	.534	.535	:536	1537

	ſ			T				41						T	T	T				T	
5		U	rnthetase bet			ansferase		semialdehyde	ansferase	otransferase	nthetase		se		.			e (tyrosine			9
10		Function	phenylalanyl-tRNA synthetase beta chain		esterase	macrolide 3-O-acyltransferase		N-acetyiglutamate-5-semialdehyde dehydrogenase	giutamate N-acetyltransferase	acetylornithine aminotransferase	argininosuccinate synthetase		argininosuccinate lyese				nypothetical protein	tyrosyl-tRNA synthase (tyrosine tRNA ligase)	hypothetical protein		hypothetical protein
15		Matched length (a.a.)	343		363	423		347	388	391	401		478			_	20	417	149		45
20		Similarity (%)	7.17		55.1	56.3		99.1	99.7	99.2	99.5		0.06				72.0	9.62	64.4		75.0
. ,		Identity (%)	42.6		26.5	30.0		98.3	39.5	99.0	99.5		83.3			:	48.0	48.4	26.9		71.0
25	(pa	-	655		A	ens		۳n.	mn:	Œ,	m		Ę								5
	Table 1 (continued)	Hamalogous gene	Escherichia coli K12 MG1655 syfB		S:reptomyces scabies estA	S:reptomyces mycarofaciens rdm3		Corynebaclerium glutamicum ASO19 argC	Corynebaclerium glutamıcum ATCC 13032 argJ	Corynebacterium glutamicum ATCC 13032 argD	Corynebac:erium glutamicum ASO19 argG		Corynebacterium glutamicum ASO19 argH				Escherichia coil K12 ycaR	Bacillus subtilis syy1	Methanococcus jannaschii MJ0531		Chlamydia muridarum Nigg TC0129
40		db Match	sp:SYFB_ECOU		SP.ESTA_STRSC 'S	Sp:MDMB_STRMY		gp:AF005242_1	sp ARGJ_CORGL	sp:ARGD_CORGL	Sp.ASSY_CORGL		gp:AF048764_1				sp:YCAR_ECOLI	sp:SYY1_BACSU	sp:Y531_METJA		PIR:F81737
		ORF (bp)	2484	77.1	972	1383	402	1041	1164	1173	1203	1209	1431	1143	1575	612	177	1260	465	390	141
45		Terminal (nt)	1460516	1458196	1462128	1453516	1463934	1465123	1466373	1468548	147-413	1470154	1472907	1474119	1475693	1476294	1476519	1477809	14/7929	1478503	1483335
50		Initial (nt)	5038 1458133, 1460516	1458966	5040 1461157	5041 1462134	5042 1463533 1463934	5043 1464083	1455210	1457376	5046 1470211	1471362	5048 1471477	1472577	1474119	1475683	1476343	1476550	1478393	1478892	1483475
		SEO NO.	5038	5039	2040	5041	5042	5043	5044	5045	5046	5047	5048	5049	2050	5051	5052	5053	5054	5055	5056
55	*	SEO SEO NO NO (JNA) (a.a.)	1538	1539	1540	1541	1542	1543	15.44	1545	1546	1547	1548	1549	1550	1551	1552	1553	1554	1555	1556

EP 1 108 790 A2

											<del></del> т			<u> </u>			Т	-		
5	<b>L</b> D		actor IF-2								ammonia			TP-binding	oning protein or active se bacterial			ısferase		unit nase B
1 <b>0</b>	Function	hypothetical protein	translation initiation factor IF-2	hypothetical profein		hypothetical protein	hypothetical protein	DNA repair protein	hypothetical protein	hypothetical protein	CTP synthase (UTP-ammonia ligase)	nypothetical protein	tyrosine recombinase	tyrosin resistance ATP-binding protein	cnromosome partitioning protein or ATPase involved in active partitioning of diverse bacterial plasmids	hypothetical protein		thiosulfate sulfurtransferase	hypothetical protein	ribosomal large subunit pseudouridine synthase
15	Matched length (a.a.)	84	182 t	311	寸	260	225	574	394	313	549	157	300	551	258	251		270	172	229
20	Similarity (%)	0.39	0.79	60.1		9.69	31.6	63.4	73.1	68.1	7.97	71.3	7.17	59.7	73.6	64.5		67.0	65.7	72.5
	identity (%)	61.0	36.3	29.6		38.5	31.6	31.4	41.9	30.4	55.0	36.3	39.7	30.5	44.6	. 28.3		35.6	33.1	45.9
25 Q							is		sis	şiş			ő		arA					
35 Table 1 (continued)	Homologous gene	Ch'amydia pneumoniae	Borrelia burgdorferi IF2	Bacillus subtilis yzgD		Bacillus subtilis yqxC	Mycobacterium tuberculosis H37Rv Rv1695	Escherichia coli K12 recN	Nycobacterium tuberculosis H37Rv Rv1697	Nycobacterium tuberculosis H37Rv Rv1698	Escherichia coli K12 pyrG	Bacillus subtilis yakG	Staphylococcus aureus xerD	Streptomyces fradiae thC	Caulobacter crescentus parA	Bacillus subtitis ypuG		Datisca glomerata tst	Bacillus subtilis ypuH	Eacillus subtilis rluB
40	db Match	GSP: Y35814	Sp.IF2 BORBU	sp:YZGD_BACSU		sp:Yaxc_BAcsu	sp:YFJB_HAEIN	SP. RECN_ECOLI	pir.H70502	pir.A70503	sp.PYRG_ECOL!	Sp:YOKG BACSU	go AF093543 1		gp CCU87804_4	sp.YPUG_BACSU		gp:AF109155_1	SP YPUH_BACSU	sp:RLUB_BACSU
	ORF (op)	273	1353	984	162	819	873	1779	1191	963	1662	657	912	1530	783	765	198	867	543	756
45	Terminal (nt)	1483724	1486027	1487025	1487193	1488056	1489018	1490881	1492134	1493109	1495174	1495861	1496772	1496795	1499645	1500695	1500911	1502576	1503:76	1504238
50	Initial (nt)	1483936	<del></del>		1487032	1487238	1489145	1489103	1490944	1492147	1493513	1495205	1495861		5070 1498863	1499931	1501471	1501710	1502634	1575 5075 1503483
	SEO		-	1	2060		5062	5063		5005	9905	5067	_	<del></del>	5070	5071	5072		1574 - 5074	5075
55	SEO	.557	. 558	1559	1560	1561	1562	1563	1564	1565	1566	1567	1568	1569	1570	1571	1572	1573	1574	1575

5
10
15
20
 25
30
35
40
45
50

	Function	cytidylate kinase	GTP binding protein			methyl:ransferase	ABC transporter	ABC transporter		hypothetical membrane protein		Na+/H+ antiporter			hypothetical protein	2-hydroxy-6-oxohepta-2,4-dienoate hydrolase	preprotein translocase SecA subunit	signal transduction protein	hypothetical protein	hypothetical protein
	Matched length (a a)	220	435			232	499	602		257		499			130	210	805	132	234	133
	Similarity (%)	736	740			67.2	; 09	£ 95		73.2		61.5			57.7	63.8	61.7	93.2	74.4	63.2
	Identity (%)	38.6	42.8			36.2	29.7	31.2		39.7		25.7			36.9	25.2	35.2	75.8	41.9	30.8
Table 1 (continued)	Homologous gene	Bacillus subtilis cmk	Bacillus subtilis yphC			Mycobacterium tuberculosis Rv3342	Corynebacterium striatum M82B tetA	Corynebacterium striatum M82B tetB		Escherichia coli K12 ygiE		Bacillus subtilis ATCC 9372 nhaG			Escherichia ccli K12 o249#9 ychJ	Archaeoglobus fulgidus AF0675	Bacillus subtilis secA	Mycobacterium smegmatis garA	Mycobacterium tuberculosis H37Rv Rv1828	Mycobacterium tuberculosis H37Rv Rv1828
	db Match	, sp.KCY_BACSU	sp.YPHC_BACSU			sp.YX42_MYCTU	prf 25°3302B	prf 25° 3302A		sp.YGIE_ECOL!		gp:AB029555_1			sp:YCHJ_ECOLI	pir C69334	sp.SECA_BACSU	gp.AF173844_2	sp:Y0DF_MYCTU	sp.Y0DE_MYCTU
	ORF (bp)	690	1557	999	493	813	1554	1767	925	789	189	1548	186	420	375	1164	2289	429	756	633
	Terminal (n:)	1504945	1506573	1506662	1507932 1507405	1507917	1510366	1512132	1510843	1512977	1514693	1512980	1512974	1515815	1515408	1515799	1515458	1520029	1520945	152+589
	Intial (nt)	1504256	1505017	5078   1507327   1506662	1507902	5080 1508729	1508813	5082 1510366	1511667	1512189	1514505	1514527	1515159	1515396	1515782	5090 1516962	1517170	1519601	5093, 1520190	1520557
	SEO NO (a a)	5076	5077	5078	5079	5080	5081	5082	5083	5084	5085	5086	5087	5088	5089	2090	5091	5092	5093	5094
į	SEQ NO (DNA)	1576	1577	1578	1579	1580	:581	1582	1583	1584	1585	1586	1587	1589	1589	1590	1591	1592	1593	1594

EP 1 108 790 A2

10	Function	hypothetical protein					hemolysin	hemolysin		DEAD box RNA helicase	ABC transporter ATP-binding protein	6-phosphogluconate dehydrogenase	thioesterase		nodulation ATP-binding protein I	hypothetical membrane protein	transcriptional regulator	phosphonates transport system parmease protein	phosphonates transport system permease protein	phosphonates transport ATP-binding protein		
15	B c			_	_		hem	hem	_	Ä		6-ph	thior			Һурс		or q per				
	Matched length (a.a.)	178					342	65		374	245	492	121	-	235	232	772	. 281	268	250		
20	Similarity (%)	84.3					0.69	65.5		69.5	66.1	89.2	67.8	,	68.1	76.3	63.9	63.4	62.3	72.0		
	Identity (%)	71.4					33.9	31.4		41.2	34.3	0.66	39 7		.39.6	43.1	26.7	29.9	27.2	44.8		
25 <del>Q</del>		v								4	s		s			S						
os Table 1 (continued)	Homologous gene	Mycobacterium tubercutosis H37Rv Rv1828					Bacilus subtilis yhdP	Bacillus subtilis yhdT		Thermus thermophilus herA	Mycobacterium tuberculosis H37Rv Rv1348	Brevibacterium flavum	Mycobacterium tuberculosis H37Rv Rv1847		Rhizobium sp. N33 nodl	Mycobacterium tuberculosis H37Rv Rv1686c	Escherichia coli K12 yfhH	Escherichia coli K12 phnE	Escherichia coli K12 phnE	Escherichia coli K12 phnC		
35												ш	42 T			<b>≥</b> ⊥						
40	db Match	sp:Y0DE_MYCTU					Sp:YHDP_BACSU	sp.YHDT_BACSU		go TTHERAGEN_1	sp YD48_MYCTU	gsp:W27613	pir.G70664		sp:NODI_RHIS3	pir:E70501	Sp.YFHH_ECOLI	sp:PHNE_ECOL:	sp:PHNE_ECOLI	sp PHNC_ECOLI		
	ORF (bp)	573	510	1449	009	930	1062	1380	219	1344	735	1476	462	675	741	741	873	846	8	834	210	1050
45	Termina (n.)	1522343	1522432	1523052	1525973	1524568	1525473	1526534	1528185	1527987	1530220	1530341	1532394	1532996	1533781	1534521	1534529	1535382	1536227	1537030	1538968	1537870
50	Initial (nt)	1521771	1522941	1524500	1525374	1525497	1526534	:527913	.527968	-529330	5104 1529485	1531816	1531933	1532322	1533041	1533791	1535401	5111 1536227	1537030	1537833	632863.	1538919
	SEQ NO (a a.)	5095	5096	5097	86CS	5399	5100	5101	5102	5103	5104	5105	5106	5107	5108	5109	5110	5111	5112	5113	5114	5115
55	SEQ. NO.	. 1595	. 1596	1597	1598	1599	1600	1601	1602	1603	1604	1605	1606	1607	1608	1609	1610	1611	1612	1613	1614	1615

	г	<del></del>								, T			<sub>1</sub>	Τ.		т		$\neg$	- 1		. г	т.	—- <sub>1</sub>
5		Function		phosphomethylpyrimidine kinase	hydoxyethylthiazole kinase	cyclopropane-fatty-acyl-phospholipid synthase	sugar transporter or 4-methyl-o- puthalate/phthalate permease	purine phosphoribosyltransferase	hypothetical protein	arsenic oxyanion-translocation pump membrane subunit		hypothetical protein	sulfate permease	hypothetical protein					hypothetical protein	dolichol phosphale mannose synthase	apolipoprotein N-acyltransferase		secretory lipase
15		Matched length (a.a.)		262	249	451	468	156	206	361		222	469	97					110	217	527		392
20		Similarity (%)		70.2	77.5	55.0	66.9	9.09	68.5	54.6		83.8	83.6	50.0					87.3	71.0	55.6		55.6
		Identity (%)		47.3	46.6	28.6	32.5	36.5	39.8	23.3		62.2	51.8	39.0					71.8	39.2	25.1		23.7
25 30	Table 1 (continued)	Homologous gene		Salmonella typhimurium thiD	Salmonella typhimurium LT2 thiM	Mycobacterium tuberculosis H37Rv ufaA1	Burkholderia cepacia Pc701 mopB	Thermus flavus AT-62 gpt	Escherichia coli K12 yebN	Sinorhizobium sp. As4 arsB		Streptomyces coelicolor A3(2) SCI7.33	Pseudomonas sp. R3 ORFA	Pseudomonas sp. R9 CRFG				-	Mycobacterium tuberculosis H37Rv Rv2050	Schizosaccharomyces pombe dpm1	Escherichia coli K12 Int		Candida albicans lip1
40		db Match		Sp.TH.D_SALTY	sp:THIM_SALTY	p:r.H73830	prf 2223339B	prf 2120352B	SP. YEBN_ECOLI	gp AF178758_2		gp:SCI7_33	gp:PSTRTETC1_6	GP.PSTRTETC1_7					pir.A70945	prf.2317468A	sp LNT_FCOLI		1224 gp.AF188894_1
		ORF (bp)	702	1584	834	1314	1386	474	666	966	483	693	1455	426	615	207	189	750	396	810	1635	741	1224
45		Terminal (nt)	1538963	1539820	1542119	1546289	1546307	1547967	1549349	1550398	1550951	1552237	1553972	1553297	1554070	1555067	1554891	1555086	1556771	1557014	1557859	1559497	1560437
50		Initial (nt)	1539664	1541403	1542922	.544976	5120 1547692	1548440	1548651	1549403	1550469	1551545	1552518	5127 1553722	5128 1554684	5129 1554861	5130 1555079	5131 1555835	1556376	1557823	5134   1559493	1560237	1561660
	į	SEQ NO.	5116	1617 5117	5118	5119	5120	5121	5122	5123	5124	5125	5126	5127	5128	_	_	5131	5132	5133	<u>.                                    </u>	5135	5136
55		SEQ NO. (DNA)	1616	1617	1618	1619	1620	1621	1622	1623	1624	1625	1626	1627	1628	1629	1630	1631	1632	1633	1634	1635	1636

											ase								
5		- -	ınsferase					dipeptidase		A helicase	tein transloca								
10		Function	precorrin 2 methyltransferase	precorrin-6Y C5, 15 methyltransferase			oxidoreduclase	dipeptidase or X-Pro dipeptidase		A <sup>*</sup> P-dependent RNA helicase	sec-independent protein translocase protein	hypothetical protein	hypothetical protein	hypothetical protein	hypothetical protein		hypothelical protein	hypothetical protein	hypothetical protein
15		<b>1</b> 0	pre	ĔË			Ö	. <del></del>		Ϋ́	pre	hy	ξ	hу	hy		hy	hy	ķ
		Matched length (a a)	291	411			244	382		1030	268	85	317	324	467		61	516	159
20		Similarity (%)	56.7	8.09			75.4	61.3		55.7	62.7	69.4	61.2	64.8	27.3		80.3	74.2	50.0
		Identity (%)	31.3	32.4			54.1	36.1		26.5	28.7	44.7	31.9	32.4	53.1		. 54.1	48.5	42.0
25															_				014
30	Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv cobG	Pseudornonas denitrificans SC510 cobl.			Mycobacterium tuberculosis H37Rv RV3412	Streptococcus mutans LT11 pepQ	٠.	Saccharomyces cerevisiae YJL050W dob1	Escherichia coli K12 latC	Mycobacterium leprae MLCB2533.27	Mycobacterium tuberculosis H37Rv Rv7095c	Mycobacterium leprae MLCB2533.25	Mycobacterium tuberculosis H37Rv Rv2097c		Mycobacterium tuberpulosis H37Rv Rv2111c	Mycobacterium tuberculosis H37Rv Rv2112c	Aeropyrum pernix K1 APE2014
35			ΣÏ					<u>ភ ភ</u>			ŭi .	i					ΣI	ΣI	Α.
40		db Match	pir.C70764	sp.COBL_PSEDE			sp:YY12_WYCTU	gp.AF0:4460_1		sp:WTR4_YEAST	sp:TATC_ECOU	sp.*Y34_MYCLE	sp:YY35_MYCTU	Sp:YY36_MYCLE	sp:YY37_MYCT∪		pir:B70512	pir.C70512	PIR:H72504
		CRF (bo)	774	1278	366	246	738	1137	638	2787	1002	315	981	972	1425	249	192	1542	480
45		Term nal	1562553	1562525	1564237	1564482	1564565	1565302	156/106	-567117	1569932	1571068	1571506	1572492	1573491	1575205	.574945	1575406	1577806
50		Initial (nt)	1561780	1563802	1563872	1564237	1565302	1566438	1566468	1569903	1570933	1571382	1572486	1573463	1574915	1574957	1575136	1576947 1575406	1577327
		SEQ NC (a.a.)	5137	5138	5139	5140	5141	5142	5143	5144	5145	5.46	5147	5148	5:49	5150	5151	5152	5153
55		SEQ NO (DNA)	.637	1638	629		1641	.642	1643	:644	.645	1646	.647	-648	.649	:650	, 65:	.652	:653

																			_
5		c	chaperone-like	đ,	est		protein	rotein	ase	ansferase	utase	ate Iransferase		eductase	ırotein				etase
10		Function	AAA family ATPase (chaperone-like function)	protein-beta-aspartate methyltransferase	aspartyl aminopeptidase	hypothetical protein	virulence-associated protein	quinolon resistance protein	aspartate ammonia-lyase	ATP phosphor bosyltransferase	beta-phosphoglucomutase	5-methyltetrahydrofolate homocysteine methyltransferase		alkyl hydroperoxide reductase subunit F	arsenical-resistance protein	arsenate reductase	arsenate reductase		cysteinyl-tRNA synthetase
15		Matched length (a.a.)	545	281	436	269	69	385	526	281	195	1254		366	388	129	123		387
20		Similarity (%)	78.5	79.0	67.2	71.4	72.5	61.0	93.8	5.76	63.1	62.4		49.5	63.9	64.3	75.6		64.3
	e de la	Identity (%)	51.6	57.3	38.1	45.4	40.6	21.8	8.66	96.8	30.8	31.6		22.4	33.0	32.6	47.2		35.9
25	(pa		s arc	πŢ		sis	198	orA23	cum MJ233	د n س	88	Ť		: ahpF	je.	lasmid	sis		(0)
<i>30</i>	Table 1 (continued)	Homologous gene	Rhodococcus erythropolis arc	Mycobacterium leprae pim T	Homo sapiens	Mycobacterium tuberculosis H37Rv Rv2119	Dichelobacter nodosus A198 vapl	Staphylococcus aureus norA23	Corynebacterium glutarnicum (Brevibacterium flavum) MJ233 aspA	Corynebacterium glutamicum ASO19 hisG	Thermo:oga maritima MSB8 TM1254	Escherichia coli K12 melH		Xanthomonas campestris ahpF	Saccharomyces cerevisiae S288C YPR201W acr3	Staphylococcus aureus plasmid pl258 arsC	Mycobacterium tuberculosis H37Rv arsC	,	Escherichia coli K12 cysS
33		5	<del>!</del> !																
40		db Match	prf.24223820	pir.S72844	gp:AF005050_1	oir:B70513	sp:VAPI_BACNO	prf.2513299A	sp.ASPA_CORGL	gp:AF050166_1	pir:H72277	sp:METH_ECOL!		1026 sp.AHPF_XANCH	sp:ACR3_YEAST	sp ARSC_S"AAU	pir:G70964		12 sp SYC_ECOLI
		CRF (bp)	1581	834	1323	834	264	1209	1578	843	693	3663	570	1026	1176	420	639	378	1212
45		Term ral (nt)	1576951	1578567	1579449	1581640	1582114	1582273	1583913	1595603	1586812	1587573	1591912	1591941	1594512	1594951	1595668	1595844	1596249
50		fritial (nt)	1578531	1579400	1580771	1580807	1581851	1583481	1585490	1586445	1587504	1591235	:591343	1592966	.593337	1594532	1595030	1596221	1597450
	a.	SEQ NO (a a.)	5154	5155	5156	5157	5158	5159	5160	5161	2915	5163	5154		5168	5167	5168	5169	5170
55	انچمسر :	SEQ NO.	1654	:655	1655	.657	1658	1659	1660	1661	1552	1563	1564	1565	1666	1667	1668	1669	1670

methylmalonyl-CoA mutase alpha subunit

741

87.5

72.2

Streptomyces cinnamonensis A3823.5 mutB

2211 SP.MUTB\_STRCM

1512234

1588 | 5188 | 1614444

	ſ	<del></del>	T	T		T	Ţ			$\neg$	etic	दु			T					-
5		Function	bacitracin resistance protein	oxidoreductase	lipoprotein	dihydroorotate dehydrogenase			fransposase		bio operon ORF I (biotin biosynthetic enzyme)	Neisserial polypeptides predicted to he useful antigens for vaccines and diagnostics		ABC transporter		ABC transporter		puromycin N-acetyltransferase	LAO(lysine, arginine, and ornithine)/AO (arginine and ornithine)transport system kinase	
15		Matched length (a.a.)	255	326	359	334			360		152	198		597		535		56	339	_
20		Similarity (%)	69.4	62.6	53.5	67.1			55.3		75.0	33.0		68.7		67.1		56.4	723	
		Identity (%)	37.3	33.4	27.0	44.0			34.7		44.1	26.0		43.6		36.8		32.4	43.1	Ĺ
25	inued)	ene	acA	ciens	ulosis	1			e trpA		rbhB	_		ıtum M82B		itum M82B		s pac	ırgK	
	Table 1 (continued)	Homologous gene	Escherichia coli K12 bacA	Agrobacterium tumefaciens mocA	Mycobacterium tuberculosis H37Rv lppL	Agrocybe aegerita ura1			Pseudomonas syringae trpA		Escherichia coli K12 ybhB	Neisser.a meningitidis		Corynebacterium striatum M82B tetB		Corynebacterium striatum M82B tetA		Streptomyces anulatus pac	Escherichia coli K12 argK	
40		db Match	sp.BACA_ECOLI	prf.2214302=	pir.F70577	Sp.PYRD_AGRAE			gp.PSESTBCBAD_1		sp:YB-4B_ECOLI	GSP:Y74829		pf 2513302A		87 prf.2513302B		19 (pir.JU0052	1089 sp.ARGK_ECOLI	
		ORF (bp)	879	948	666	1113	351	807	1110	488	531	729	63	1797	249	1587	351	609	1089	
45		Terminal (nt)	1597745	1599614	1600677	1501804	1501931	1603466	1504629	1604830	1505281	1506689	1608248	1505861	1609335	1507661	1509842	1610844	1511150	
50		nitial (nt)	1598623	1598667	1599679	1600692	1602281	1602660	1603520	:605315	1605811	1605961	1607645	1607657	1609087	1639247	1610192	.610236	:612238	
		SEQ NO.	5171	5172	5173	5174	5175	5175	5177	5178	5179	5180	5181	5182	5183	5184	5185	5186	1687 5187	
55		SEQ NC (DNA)	1671	1672	1573	1674	1675	1576	1577	1578	1679	1680	1681	1682	1683	1684	1685	1586	1687	

hypothetical protein

446

86.1

61.2

Neisseria meningitidis MC58 NMB1652

\*633324 1392 gp: AE002515\_9

5205 1631933

1631353 393

5		c	iutase beta	ne protein		ne protein	se protein							Of.				
10		Function	methylmalonyl-CoA mutase beta subunit	hypothetical membrane protein		hypothetical membrane protein	hypothetical membrane protein	hypothetical protein		ferrochelatase	invasin		aconitate hydratase	transcriptional regulator	GMP synthetase	hypothetical protein	hypothetical protein	
15		Matched length (a.a.)	610	224		370	141	261		364	611	•	959	174	235	221	98	
20		Similarity (%)	68.2	70.1		87.0	78.7	72.8		65.7	56.5		85.9	81.5	51.9	62.0	80.2	
		Identity (%)	41.6	39.7		64.1	44.7	51.0		36.8	25.5		6.69	54.6	21.3	32.6	37.2	
25	(inued)	lene	onensis	culosis		culosis	culosis	lor A3(2)		uden:reichli nH	۴	. —	culosis	culosis	ıschii	lor A3(2)	schii	
30 35	Table 1 (continued)	Homologous gene	Streptomyces cinnamonensis A3823.5 mutA	Mycobacterium tuberculosis H37Rv Rv1491c		Mycobacterium tuberculosis H37Rv Rv1488	Mycobacterium tuberculosis H37Rv Rv1487	Streptomyces coelicolor A3(2) SCC77.24		Propionibacterium freudenzeichl subsp. Shermanii hemH	Streptococcus faecium		Mycobacterium tuberculosis H37Rv acn	Mycobacterium tuberculosis H37Rv Rv1474c	Methanococcus janraschli WJ1575 guaA	Streptomyces coelicolor A3(2) SCD82.04c	Methanococcus jannaschii MJ1558	
40		db Match	sp:MUTA_STRCM.	sp:YS13_MYCTU		sp:YS39_MYCTU	p.rB70711	gp.SCC77_24		sp HEMZ_PROFR	sp.P54_ENTFC		pir F73873	pir E70873	pir F54496	gp:SCD82_4	pir.E64494	
		ORF (bp)	1848	723	597	1296	435	843	783	1110	1800	498	2829	564	756	663	267	
45		Terminal (nt)	1614451	1617300	1617994	1518321	1519672	1620167	1621838	1621841	1623027	1625428	1629107	1629861	1630668	1630667	1631926	
50		Initial (nt)	1616298	16.6578	.617398	1619616	1620106	1621009	1621056	5196 1622950	1624826	5198 1625925	5199 1626279	5200 1629298	1629913	5202 1631329	1631660 1631926	
		SEQ NO.	5189	5130	5191	5192	5193	5194	5195		5137	5198			5201	5202	5203	
55		SEQ NO.	1689	1690	1691	1692	1693	1694	1695	1696	1697	1698	1699	1700	1701	1702	1703	!
								•	•		-,							

5	Function	antigenic protein	antigenic protein	cation-transporting ATPase P		hypothetical protein					host cell surface-exposed lipoprotein	integrase	ABC transporter ATP-binding protein		sialidase	transposase (IS1628)	transposase protein fragment	hypothetical protein		dTDP-4-keto-L-rhamnose reductase	nitragen fixation protein
15	Matched length (a.a.)	113	152	883		120					107	154	497		387	236	37	88		107	149
20	Similarity (%)	0.09	0.69	73.2		58.3			į.		73.8	60 4	64 4		72.4	100.0	72.0	43.0		70.1	85.2
	Identity (%)	54.0	59.0	42.6		35.8					43.0	34.4	32.8		51.9	9.66	64.0	32.0		32.7	63.8
25 Onlined)	gene	eae ORF24	eae	CC6803		color A3(2)					nophilus	int	2 yijK		ndifaciens	Lıtamicum AG1 tnpB	Ltamicum			Orsay	rae 7
& Table 1 (continued)	Homologous gene	Neisseria gonorrhoeae	Neisseria gonorrhoeae	Synechocystis sp. PCC6803 sll1814 pma1		Streptomyces caelicalor A3(2) SC3D11.02c					Streptococcus thermophilus phage TP-J34	Corynephage 304L int	Escherichia coli K12 yijK		Micromonospora vindifaciens ATCC 31146 nedA	Corynebacterium glutamicum 22243 R-plasmid pAG1 tnpB	Corynebacterium glutamicum TnpNC	Plasmid NTP16		Pyrococcus abyssi Orsay PAB1C87	Mycobacterium leprae MLCL536.24c nifU7
35 40	db Match	GSP: Y38838 h	GSP:Y38838 N	sp.ATA1_SYNY3		gp:SC3D11_2					pri:2408488H	prf-2510491A	sp:YJJK_ECOLI [		Sp.NANH_MICVI	gp:AF121000_8	GPU.AF164956_23	GP:NT1TNIS_5		pir B75015	pir.S72754
	ORF (bp)	+	456	2676	783	489	1362	357	156	162	375	456	1629	1476	1182	708	243	261	585	423	447
45	Terminal (nt)	:632109	1632682	.635241	1633781	.636244	1638442	1638775	1639520	1639817	1640155	1641001	1641046	1642743	1644318	1646368	1646063	1645601	1647133	1547212	1647651
50	Initial (nt)	1632588	1633137	1633566	1634563	1636732	1637381	1639132	1639365	1639656	163978:	1640546	1642674	1644218	1645499	1645661	1645821	1645861	1723 5223 1646549	-647634	-648097
	SEQ NO.		5207	5208	5209	1710 5210	5211	5212	5213	5214	5215	5216		5213	5219	5220	5221	5222	5223	1724 : 5224	1725 : 5225
برر 55	SEQ.	1706	1707	1738	1709	1710	1711	1712	1713	1714	1715	1716	1717	1718	1719	1720	1721	1722	1723	1724	1725

5	Function	hypothetical protein	nitrogen fixation protein	ABC transporter ATP-binding protein	hypothetical protein	ABC transporter	DNA-binding protein	hypothetical membrane protein	ABC transporter	hypothetical protein	hypothetical protein		helicase	quinone oxidcreductase	cytochrome o ubiquinol oxidase assembly factor / heme O synthase	transketolase	transaidolase	
15	Matched length (a.a.)	52	4.1	252	377	493	217	518	317	266	291		418	323	295	875	358	
20	Similarity (%)	57.0	84.4	89.3	83.0	73.0	71.4	87.8	77.3	74.8	748		51.0	6.07	8.99	100.0	85.2	
	Identity (%)	48.0	64.7	70.2	55.2	41.0	46.1	36.3	50.2	41.0	43.0		23.4	37.5	37.6	100.0	62.0	
S G Table 1 (continued)	Homologous gene	Aeropyrum pernix K1 APE2025	Mycobacterium leprae nifS	Streptomyces coeilcolar A3(2) SCC22.04c	Mycobacterium tuberculosis H37Rv Rv1462	Synechocystis sp. PCC6803 slr0074	Streptomyces coelicolor A3(2) SCC22.08c	Mycobacterium tuberculosis H37Rv Rv1459c	Mycobacterium leprae MLCL536.31 abc2	Mycobacterium leprae MLCL536.32	Mycobacterium tuberculosis H37Rv Rv1456c		Pyrococcus horikoshii PH0450	Escherichia coli K12 qor	Nitrohacter winogradskyi coxC	Corynebacterium glutamicum ATCC 31833 धिर	Mycobacterium leprae MLCL536.39 tal	
40	db Malch	PIR:C72506	pir.S72761	gp.SCC22_4	pir.A70872	sp:Y074_SYNY3	gp.SCC22_8	pir.F70871	0 pir.S72783	pir.S72778	pir.C70871		pir.C71156	sp:doR_ECOLI	gp:NWCOXABC_3	gp:AB023377_1	Sp.TAL_MYCLE	
	ORF (bp)	162	1263	756	176	:443	693	1629	. 1020	804	666	357	1629	975	696	2100	1080	1164
45	Terminal (~t)	1648709	1648100	1649367	1650249	1651433	1652894	1655671	1656700	1657515	.658675	1659140	1661136	1662552	1662630	1666502	1667752	$\neg$
50	Initial (nt)	1648548	1649362	1650122	1651424	1652875	5231 1653586	5232 1654043	1655681	5234 1656712	1657677	1659496	1659508	1661578	5239 1663598	1664403	1666673	1667764 1666601
	SEQ NO. (a.a)	5226	5227	5228	5229	5230	5231	5232	5233	5234	5235	5236	5237	5238	5239	5240	5241	5242
55	SEQ NO. (DNA)	1726	1727	1728	1729	1730	1731	1732	1733	1734	1735	1736	1737	1738	1739	1740	1741	1742

EP 1 108 790 A2

																	T		
5		Function	glucose-6-phosphale dehydrogenase	oxppcycle protein (glucose 6- phosphate dehydrogenase assembly protein)	6-phosphogluconolactonase	sercosine oxidase	transposase (IS16/6)	sarcosine oxidase				triose-phosphate isomerase	probable membrane protein	phosphoglycerate kinase	glyceraldehyde-3-phosphate dehydrogenase	hypothetical protein	hypothetical protein	hypothelical protein	excinuclease ABC subunit C
15		Matched length (a a.)	484	318		$\neg$	200	205			1	259	128	405	333	324	309	281	701
20		Similarity (%)	100.0	71.7	58.1	57.8	46.6	100.0				9.66	51.0	98.5	99.7	87.4	82.5	76.2	61.5
v.	to the second	Identity (%)	96.8	40.6	28.7	35.2	24.6	100.0				99.2	37.0	98.0	99.1	63.9	. 56.3	52.0	34.4
25	ntinued)	ene	E	rculosis A	evisiae o.3		opolis	utamıcum				u:amicum 9 tpiA	revisiae	utamicum 9 pgk	lutamicum 9 gap	erculosis	erculosis	erculosis	Pcc6803
30	Table 1 (continued)	Homologous gene	Brev:bacterium flavum	Mycobacterium tuberculosis H37Rv Rv1446c opcA	Saccharomyces cerevisiae S288C YHR163W so.3	Bacillus sp. NS-129	Rhodococcus erythropolis	Corynebacterium glutam:cum ATCC 13032 soxA				Corynebacterium glu:amicum AS019 ATCC 13059 tpiA	Saccharomyces cerevisiae YCR013c	Corynebacterium glutamicum AS019 ATCC 13059 pgk	Corynebacterium glutamicum AS019 ATCC 13059 gap	Mycobacterium tuberculosis H37Rv Rv1423	Mycobacterium tuberculosis H37Rv Rv1422	Mycobacterium tuberculosis H37Rv Rv1421	Synechacyslis sp. PCC6803 uvrC
35 40		db Match	gsp:W27612 B	M Pir.A70917 H	sp SOL3_YEAST S	Sp.SAOX_BACSN B	1401 gp. AF126281_1 R	5				sp:TPIS_CORGL	SP.YCQ3_YEAST	sp.PGK_CORGL	sp.G3P_CORGL	pir.D70903	sp:YR40_MYCTU	sp:YR39_MYCTU	sp.UVRC_PSEFL
		ORF (bp)	1452 g	256	705	405	1401	840	174	687	981	777	408	1215	1002	981	1023	927	2088
45		Termiral (nt)	1669401	1670375	1671099	1671273	:673123	1673266	1677384	1678070	1580128	1693332	1681670	1681190	1582624	1684117	1585115	1586152	1687103
50		Iritial (1r)	1667550 1669401	1669419 1670375	1670395	1671677	1671723	1674105	1677211	1678756	1679148	1681108	1681263	1682404	1683625	1685097	1686132	1687078	5259 1689190
		SEO	(a.a.) 5243	5244	5245	5246	5247		5249	5250	5251	5252	5253	5254	5255	5256	5257	1758 5258	•
<i>55</i>		SEO	1743	1744	-745	.745	:747	1748	1749	1750	1751	1752	1753	1754	1755	1756	1757	1758	1759

5
10
15
20
 25
30
35
40
45
50

	Function	hypothetical protein	6,7-dimethyl-8-ribityllumazine synthase	polypeptide encoded by rib aperon	riboflavin biosynthetic protein	polypeptide encoded by rib operon	GTP cyclohydrolase II and 3, 4- dihydroxy-2-butanone 4-phosphate synthase (riboflavin synthesis)	riboflavin synthase alpha chain	riboflavin-specific deaminase	ribulose-phosphate 3-epimerase	nucleolar protein NOL 1/NOP2 (eukaryotes) family	methionyl-IRNA formyltransferase	polypeptide deformylase	primosomal protein n'	S-adenosylmethionine synthetase	ONA/oantothenate metabolism flavoprotein	hypothetical protein	guanylate kinase	integration host factor
	Matched length (a.a.)	150	154	72	217	106	404	211	365	234	448	308	150	725	407	409	81	186	103
	Similarity (%)	2'89	72.1	0.89	48.0	52.0	84.7	79.2	62.7	73.1	60.7	6.73	72.7	46.3	99.5	80.9	7.78	74.7	90.3
	Identity (%)	32.7	43.5	59.0	26.0	44.0	.65.6	47.4	37.3	43.6	30.8	41.6	44.7	22.9	99.3	58.0	70.4	39.8	80.6
Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv1417	Escherichia coli K12	Bacillus subtilis	Bacillus subtilis	Bacillus subfilis	Mycobacterium tuberculosis ribA	Actinobacillus pleuropneumoniae ISU-178 ribE	Escherichia co'i K12 r·bD	Saccharomyces cerevisiae S288C YJL121C rpe1	Escherichia coli K12 sun	Pseudomonas aeruginosa fmt	Bacillus subtilis 168 def	Escherichia coli priA	Brevisacterium flavum MJ-233	Mycobacterium tuberculosis H37Fv RV1391 dfp	Mycobacterium tuberculosis H37Rv Rv1390	Saccharomyces cerevisiae guk1	Mycobacterium tuberculosis H37Rv Rv1388 m!HF
	db Match	sp:YR35_MYCTU	sp:RISB_ECOLI	GSP.Y83273	GSP Y83272	GSP:Y83273	gp.AF001929_1	Sp.RISA_ACTPL	sp.RIBD_ECOLI	sp:RPE_YEAST	sp:SUN_ECOLI	sp:FMT_PSEAE	sp.DEF_BACSU	Sp. PRIA_ECOLI	gsp:R80060	sp:DFP_MYCTU	Sp:YD90_MYCTU	pir.KIBYGU	pir.B70899
	ORF (bp)	579	477	228	714	335	1266	533	984	557	:332	945	507	2064	1221	1260	291	627	3,8
,	Terminal (nt)	1689201	1689869	1690921	1691421	1691347	1693360	1691639	1692275	1693262	1693967	1695499	1596466	1697084	1699177	1700508	1702322 1702032	1702411	1702991
	Initial (nt)	1689779	1690345 1689869	1690654	1590708	1691012	1691625	1692271	1693258	1693918	1695298	1696443	1696972	1699147	1700397	1701757		1703037	1703308
	SEQ NO (9 8 )	5260	5261	5262	5263	5264	5265	5266	5267	5268	5269	5270	5271	5272	5273	5274	5275	5276	5277
	SEQ NO.	1760	1761	1762	1763	1764	1765	1766	1767	1768	1769	1770	1771	1772	1773	1774	1775	1775	222.

5			Function	orotidine-5'-phosphate decarboxylase	carbamoyl-phosphate synthase large chain	ca-bamoyl-phosphate synthase small chain	dihydroorotase	aspartate carbamcyltransferase	phosphoribosyl transferase or pyrimidine operon regulatory protein	cell division inhibitor				N utilization substance protein B (regulation of rRNA biosynthesis by transcriptional antitermination)	elongation factor P	cytoplasmic peptidase	3-dehydroquinate synthase	shikimate kinase	type IV prepilin-like protein specific leader peptidase
15			Matched length (a a)	276 or	1122 ca	381 ca	402 di	311 as	176 97;	297 56				137 TE	187 el	217 C	361 3	166 s	142 (1)
20			Similarity (%)	73.6	77.5	70.1	67.7	79.7	80.1	73.4	-		-	69.3	98.4	100.0	2.66	100:0	54.9
	•		Identity (%)	51.8	53.1	45.4	42.8	48.6	54.0	39.7		•		33.6	97.9	99.5	98.6	100.0	35.2
30		Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv uraA	Escherichia coli carB	Pseudomonas aeruginosa ATCC 15692 carA	Bacillus caldolylicus DSM 405 pyrC	Pseudomonas aeruginosa ATCC 15692	Bacillus caldolyticus DSM 405 pyrR	Mycobacter um tuberculosis H37Rv Rv2216				Bacillus subtilis nusB	Brevibacterium lactofermentum ATCC 13869 efp	Corynebacterium glutamicum AS019 pepQ	Corynebacterium glutamicum AS0 19 aroE	Corynebacterium glutamicum ASO:9 aroK	Aeromonas hydrophila tapD
35 40			db Match	SP. DCOP_MYCTU	pir.SYECCP E	SP.CARA_PSEAE	41 Sp.PYRC_BACCL	SP.PYRB_PSEAE	SP. PYRR_BACCL	SP.YOOR_MYCTU				sp:NUSB_BACSU	sp:EFP_BRELA	gp:AF124600_4	gp:AF124600_3	gp AF124600_2	Sp.LEP3_AERHY
			ORF (bp)	834	3339	1173	1341	936	576	1164	477	<b>c</b> 62	210	68:	561	1089	1095	492	4-1
45			Terminal (nt)	1703517	1704359	1707706	1709017	1710413	1711352	1713759	1714306	1714760	1714950	1715382	1716:32	1716780	1717938	1719107	1720971
50			Initial (rt)	1704350	1707697	1708884	1710357	5282 1711349	1711927	1712596	1713830	1714299	1714741	1716052	1716692	17-7868	1719032	1719598	:721381
			SEQ	·	5279	5280	5281	5282	5283	5284	5285	5286	5287	5289	5289	5290	5291	5232	5293
55			SEQ NO.		1779	1780	1381	782	1783	1784	:785	:786	1787	.788	.789	062.	162;	1792	1793

5			tein, arsR			f, stein	TP-binding	nase	-		83			ıse		sidase			
10		Function	bacterial regulatory protein, arsR family	ABC transporter		iron(III) ABC transporter, periplasmic-binding protein	ferrichrome transport ATP-binding protein	shikimate 5-dehydrogenase	hypothetical protein	hypothetical protein	alanyi-IRNA synthetase	hypothelical protein		aspartyl-tRNA synthetase	hypothelical protein	glucan 1,4-alpha-glucosidase	phage infection protein		transcriptional regulator
15		Matched length (a.a.)	83	340		373	230	259	395	161	894	454		591	297	839	742		192
20		Similarity (%)	68.7	73.2		20.7	71.7	0.09	70.1	69.6	71.8	84.8		89.2	74.1	53.6	54.0		62.0
		Identify (%)	45.8	35.9		23.6	38.3	20.0	41.8	52.8	43.3	65.4		71.1	46.1	26.1	23.1		29.2
25	ontinued)	s gene	color A3(2)	iphtheriae		Orsay	9 Pruc	erculosis	erculosis	erculosis	xidans ATCC	erculosis		rae aspS	oerculosis	erevisiae ta 1	gE		icolor A3(2)
30	Table 1 (continued)	Homologous gene	Streptomyces coelicolor A3(2) SC1A2.22	Corynebacterium diphtheriae hmuU		Pyrococcus abyssi Orsay PAB0349	Bacil'us subtilis 168 fhuC	Mycobacterium tuberculosis H37Rv aroE	Mycobacterium tuberculosis H37Rv Rv2553c	Mycobacterium tuberculosis H37Rv Rv2554c	Thiobacillus ferrooxidans ATCC 33020 alaS	Mycobacterium tuberculosis H37Rv Rv2559c		Mycobacterium leprae aspS	Mycobacterium tuberculosis H37Rv Rv2575	Saccharomyces cerevisiae S288C YIR019C sta1	Bacillus subtilis yhgE		Streptomyces coelicolor A3(2) SCE68.13
<i>35</i>		db Match	gp:SC1A2_22 S	gp:AF109162_2 h	i :	pir.A75169 P	SP.FHUC_BACSU B	pir.D70660	pir.E70660	pir.:770660	sp.SYA_THIFE	sp:Y0A9_MYCTU		SP. SYD_MYCLE IN	Sp.Y08Q_MYCTU	SP.AMYH_YEAST	sp:YHGE_BACSU		gp:SCE68_13
		ORF (bp)	303	1074	909	957	753	828	1167	546	2664	1377	1224	1824	891	2676	1857	648	594
45		Terminal (nt)	172:423	1722853	1722202	1723826	1724578	1724612	1725459	1725625	1727385	1730166	1731599	1732988	1735946	1736004	1738713	1740572	1741313 1741906
50		Initial (nt)	.721725	1721780	1722807	1722870	1723826	1725439	1726625	1727170	1730248	1731542	1732922	1734811	1735056	1738679	1740539!	1741219 1740572	<u> </u>
		SEQ NO	5294	5295	5296	5297	5299	5299	5300	5301	802 5302	803   5303	5304	5305	5306	5307	5308	5306	53:0
55		SEQ.		795	796	797	798	799	900	801	802	803	1804	1805	1806	1807	1808	1809	1810

EP 1 108 790 A2

														_						_
5	Function		oxidoreductase		NADH-dependent FMN reductase	L-serine dehydratase		alpha-glycerolphosphate oxidase	histidyl-tRNA synthetase	hydrolase	cyclophilin		hypothetical protein		GTP pyrophosphokinase	adenine phosphoribosyltransferase	dipeptide transport system	hypothetical protein	protein-export membrane protein	
15	Matched length (a.a.)		371 oxide		116 NAD	462 L-sei		598 alpha	421 histic	211 hydr	175 cyclo		128 hypo		760 GTP	185 aden	49 dipe	558 nypo	332 prote	
			3.		1,	4		56	42	2,					76	18	4	25	33	
20	Similarity (%)		88.1		77.6	71.4		53.9	72.2	62.1	61.1		100.0		6'66	100.0	98.8	6.09	57.2	
	Identity (%)	·	72.8		37.1	46.8		28.4	43.2	40.3	35.4		98.4		6.66	99.5	98.0	30 7	25.9	
25 (panultured)	gene		olor A3(2)		inosa PAO1	sdaA		flavus glpO	sn	0	mailus		tamicum		g <sup>.</sup> uta:nicum	tamicum	tamicum	culosis	secF	
% % % % % % % % % % % % % % % % % % %	Homologous gene		Streptomyces coel color A3(2) SCE15, 13c		Pseudomonas aeruginosa PAO1 slfA	Escherichia coli K12		Enterococcus casseliflavus glpO	Staphylococcus aureus SR17238 hisS	Campylobacter jejuni NCTC11168 Cj0809c	Streptomyces chrysomallus sccypB		Corynebacterium gʻutamicum ATCC 13032 orf4		Corynebacterium gʻu ATCC 13032 rel	Corynebacterium glutamicum ATCC 13032 apt	Corynebacterium glutamicum ATCC 13032 dciAE	Mycobacterium tuberculosis H37Rv Rv2585c	Escherichia coli K12 secF	
35	<del>                                     </del>														8.					
40	db Match		gp:SCE15_13		sp:SLFA_PSEAE	Sp. SDHL_ECOLI		prf.2423362A		gp:CJ11168X3_12	prf:23133C9A	     	gc: AF03865*_4		gp:AF038651_	gp:AF038651_2	gp:A=038651_1	sp Y08G_MYCTU	SP SECF_ECOLI	
	ORF (bp)	714	1113	126	495	1347	861	1685	1287	639	507	1 237	555	342	2280	555	150	1743	1209	930
45	Terminal (nt)	.742606	1743813	1743968	1744519	1746230	1747588	1746233	1747990	1749325	1750933	1751200	1752051	1752527	1752615	1754925	1755599	1755486	1757599	1760336
50	Initial (nt)	1741893	174270	1743843	1744025 1744519	1744884	1746728	1747918	1749276 1747990	1749963 1749325	1750427	1750964	1751497	1752186	5324 1754894	1755479	1755748	1757228	158797	1759707
	SEQ NO (a a.)	5311	5312	5313	5314	5315	5316	5317	5318	5319	5320	532,	5322	5323	5324	5325	532E	5327	5328	5329
	SEC NO (CNA)	1811	1912	1813		1815	1816	1817	1818	1819	1820	1821	1822	1823	1824	1825	1826	1827	1828	1879

			T	_	_			-											
5	Function	protein-export membrane protein	hypothetical protein	holliday junction DNA helicase	holliday junction DNA helicase	crossover junction endodeoxyribonuclease	hypothetical protein	acyl-CoA thiolesterase	hypoth etical protein	hypothetical protein	hexosyltransferase or N- acetylglucosaminyl- phosphatidylinositol biosynthetic proteir	acyltransferase	CDP-diacylglycerolglycerol-3- phosphate phosphalidyltransferase	histidine triad (HIT) family protein	threonyl-tRNA synthetase	hypothetical profein			
15	Matched length	616	106	331	210	180	250	283	111	170	414	295	78	194	647	1	-	-	
20	Similarity (%)	52.0	66.0	81.9	74.3	63.3	78.4	9.89	61.3	61.2	49.3	67.8	78.0	78.4	68.9	51.8			-
	Identity (%)	24.4	39.6	55.3	45.2	35.6	49.2	38.5	31.5	38.2	21.7	46.4	48.2	54.6	42.0	34.3	-	-	
Table 1 (continued)	Homologous gene	Rhodobacler capsulatus secD	Mycobacterium leprae MLCB1259.04	Escherichia col: K12 ruvB	Mycobacterium leprae ruvA	Escherichia coli K12 ruvC	Escherichia coli K12 ORF246 yebC	Escherichia coli K12 tesB	Streptomyces coelicolor A3(2) SC10A5.09c	Mycobacterium tuberculosis H37Rv Rv2609c	Saccharomyces cerevisiae S288C sp114	Streptomyces coelicolor A3(2) SCL2.16c	Mycobacterium tuberculosis H37Rv Rv2612c pgsA	Mycobacterium tuberculosis H37Rv Rv2613c	Bacillus subtilis thrZ	Bacillus subtilis ywbN			
40	db Match	prf.2313285A	SD:YOBD_MYCLE	sp:RUVB_ECOLI	618 Sp. RUVA_MYCLE	sp:RUVC_ECOLI		sp. TES3_ECOLI	gp:SC10A5_9	pir H70570	sp:GPI3_YEAST	gp:SCi2_16	pir.C70571	N pir.D70571	sp.SYT2_BACSU B	SD: YWBN_BACSU B			
	ORF (bp)	1932	363	1080	618	663	753	846	474	462	1083	963	557	660	2058	1206	564	546	735
45	Terminal (nt)	1758803	1761005	1761419	1762517	1763.77	1753990	1765015	1756442	1756487	1766948	1768034	1769322	1769681	1770327	1772658	1774444	1773893	1774457
50	In tial (nt)	1760734		1762498	1763134	:763839	1764742	1765860	1765969	1766948	5339 1768030	1768996	1769678	1770340	1772384	!	5345, :773881	1774438	1775191
	SEQ NC	5330		5332	5333	5334	5335	5336	5337	5338	5335	5340	5341			5344	5345	5346	5347
55	SEQ VO (DNA)	1830	1831	1832	1833	1834	1835	1836	1837	1838	1839	1840	1841				+	-+	1847

		$ \top $						$\top$		1					_[			tein				! 	_ •		
5	Function						etyltransferase											ferric transport ATP-binding protein					etabolism		
10	ī.						puromycin N-acetyltransferase											ferric transport					pantothenate metabolism flavoprotein		
15	Matched fength (a.a.)			•			190											202					129		
20	Similarity (%)						54.2											28.7					66.7		
	identity (%)						36.3								<u></u>			28.7					27.1		
25 (panui	ane						pac											U					a		
8 Table 1 (continued)	Homologous gene						Streptomyces anulatus pac											Actinobacillus pleuropneumoniae afuC		i			Zymomonas mobilis dfp		
40	db Match						Sp.PUAC_STRLP											sp AFUC_ACTPL					gp.AF088896_20		
•	ORF (bp)	378	594	1407	615	399	267	1086	1101	669	2580	1113	1923	483	189	312	429	265	666	159	1107	420	591	864	420
45	Terminal (nt)	1777646	1778037	1778102	1779554	1780507	1781019	1782790	1784381	1783382	1782894	1785732	1786907	1789562	1789769	1790057	1790461	1792438	1793426	1793496	1794820	1795621	1796181	1797049	1797769
50	Initial (nt)	1777269	1777444	1779508	.780158	5352 1780905	5353 1781585	1781705	1783281	1784080	5357 1785473	1786844	1788829	1789090	1789580	1789746	1790889	5364 1791842	1792428	1793654	1793714	1795202	1795591	1756186	1797350
	SEO NO.	5348	5349	5350	5351	5352	5353	5354	5355	5356		5358	5359	5360	5361	5362	5363		5365	5366	5367	5368	5369	5270	5:17
<i>55</i>	SEQ NO (DNA)	1848	1849	1850	1851	1852	1853	1854	1855	1856	1857	1858	1859	1860	1861	1862	1863	1864	1865	1866	1867	1868	1869	1870	1871

												_														
5																					lvase			hatase		
10		Function																			transposon TN21 resolvase			protein-tyrosine phosphatase		
15		Matched length (a.a.)																			186			164		
20		Similarity (%)																			78.0			51.8		
		Identity (%)																			51.1			29.3		
25	ned)																				 			9		
30	Table 1 (continued)	Homologous gene																			Escherichia coli tnpR			Saccharomyces cerevis:ae S288C YIR026C yvh1		
35			-	<u> </u>	<u> </u> 	L	-	-		<u> </u>  -	-		_	_		_	_		_	_	Escl	_	<u></u>	Sac S28		
40		db Match																			sp.TNP2_ECOL!			Sp:PVH1_YEAST		
.*		ORF (bp)	120	/35	225	894	156	474	753	423	289	429	465	237	681	096	480	68,	285	375	612	1005	375	47.7	726	423
45		Term·nal (nt)	1797850	1798023	1799406	1800366	1800449	1801307	1802096	1802155	1803419	1803893	1804598	1804865	1805599	1806586	1807396	1808113	1808421	1808832	1810372	1811545	1811938	1812691	1313606	1912460
50		fnitial (nt)	1797969	1798757	1799182	1799473	1800604	1800834	1801344	1802577	1802733	1803465	1804134	:804629	1804919	1805727	.805917	1807433	1808137	1808458		1810541	5392 1811564	1812215	1812881	1812882
	أتتمس	SEQ NO.	5372	5373	5374	5375	5376	5377	5378	5379	5380	5381	5382	5383	5384	5385	5386	5387	5388	5389		5391	5392	5393	5394	5395
55		SEQ NO. (DNA)	1872	1873	1874	1875	1876	1877	1878	1879	1880	1881	1882	1883	1884	1885	1886	1887	1889	1889		1891	1892	1893	1894	1895

EP 1 108 790 A2

	1			-	_						_		$\overline{}$		r-	$\overline{}$	-							
5		Function	sporulation transcription factor									hypothetical protein					hypothetical protein	insertion element (IS3 related)	insertion element (IS3 related)			single-stranded-DNA-specific exonuclease		primase
15		Matched length (a.a.)	216									545					166	298	101			622		381
20		Similarity (%)	65.7		-							55.2					75.0	95.6	84.2			50.6		£4.3
		Identity (%)	34.3			-						22.6					63.0	87.9	72.3			24.0		31.8
25	ntinued)	gene	olor A3(2)		-							a MSB9					ıtamicum	ıtamicum	ıtamicum			ni recJ		e phi-01205
30	Table 1 (continued)	Homologous gene	Streptomyces coelicolor A3(2) whiH									Thermo:oga maritima MSB9 TM1189					Corynebacterium glutamicum	Corynebacterium glutamicum orf2	Corynebacterium glutamicum orf 1			Erwinia chrysanthemi recJ		Streptococcus phage phi-O1205 ORF13
<i>35</i>		db Match	gp:SCA32WHIH_6									pir.C72285					PIR S60891	pir.S60890	pir.S60889			sp.RECJ_ERWCH		pir.T13302
		ORF (bp)	738	789	456	186	672	417	315	369	207		1746	219	144	429	534	894	294	213	1299	1878	780	1650
45		Terminal (:nt)	1814517	1815651	1815128	1816636	1817803	1818219	1818774	1819166	1819748	1820181	1824322	1824589	1824927	1825178	1826557	1825751	1826644	1829688	1832063	1834044	1834149	1838324
50		Initial (nt)	1813780	1814863	1815673	18-6451	1817132	1817803	1818460	1818798	18:9954	1822382	1822577	1824371	1824784	1825606	1826024	1826644	1826937	1829900	1830765	1832167	1834928	5417 1836675
		SEO NO (a.a)	5356	5397	5398	5366	5400	5401	5402	5403	5404	5405	5406	5407	5408	5409	5410	5411	5412	5413	5414	5415	5416	5417
55	•	SEQ. NO. (DNA)	1896	1857	1858	1899	1900	1901	.902	1903	-604	306:	1906	1907	806,	606	919	1611	1912	1913	1914	1915	1916	1917

5	Function				helicase		phage N15 protein qp57										actin binding protein with SH3 domains					A*P/GTP binding protein		ATP-dependent Clp proteinase ATP-binding subunit
15	Matched length				620		109		      _								422					347		630
<b>20</b>	Similarity (%)				44.7		64.2										49.8					52.5		61.0
	Identity (%)				22.1		36.7										28.7					23.6		30.2
25 (continued) 1 able 1	Homologous gene				Mycoplasma preumoniae ATCC 29342 yb95		Bacteriophage N15 gene57										Schizosaccharomyces pombe SPAPJ760.02c					Streptomyces coelicolor SC5C7.14		Escherichia coli K12 cipA
40	db Match				sp:YC18_MYCPN		pir:T13144										9p:SPAPJ760_2					gp:SC5C7_14		1965 sp. CLPA_ECOLI
	ORF (bp)	3789	447	534	1839	375	336	366	618	537	529	798	186	372	438	576	1221	852	1395	594	180	1257	1854	1965
45	Terminal (nt)	1842137	184268	1843337	1845356	1845857	1846207	1846332	1847932	1848474	1849036	1849785	1849966	1850406	1849978	1850474	1852440	1852324	1853873	1854854	1855237	1856788	1858738	1860727
50	Initial (nt)	1838349	1842235	1842804	1843518	1845483	1845872	1846698	1847315	1847938	848509	.848988	:849781	1850035	1850415	1851049	5433 1851220	1851473	1852479	1854261	1855058	1855532	1856885	1958763
	SEQ NO (a.a.)	5418	5419	5420	5421	5422	5423	5424	5425	5426	5427	5428	5429		5431	5432		5434	5435	5436	5437	5438	5439	5440
55	SEQ NO (DNA)	1918	1919	1920	1921	1922	1923	1924	1925	1925	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	1538	1939	1940

	$\overline{}$			_											_	$\overline{}$							
10	Function						ATP-dependent helicase					hypothetical protein	deoxynucleotide monophosphate kinase	-				type II 5-cytosoine methyltransferase	type II restriction endonuclease			hypothetical protein	
15	Matched	(a.a.)					693					224	208					363	358			504	
20	Similarity	(%)					45.9					47.8	61.5					99.7	99.7			45.8	
	Identity	(%)					21.4					25.9	31.7					99.2	99.7			24.6	
25 (panujiuo	Spene	, n					reus SA20					color A3(2)	C31 gp52					lutamicum	lutamicum			color A3(2)	
So Continued)	Homologous gene	n	٠	,			Staphylococcus aureus SA20 pcrA					Streptomyces coelicolor A3(2) SCH17.07c	Bacteriophage pri-C31 gp52					Corynebacterium glutamicum ATCC 13032 cgllM	Corynebacterium glutamicum ATCC 13032 cgllR			Streptomyces coelicolor A3(2) SC1A2.16c	
<i>40</i>	db Watch						sp.PCRA_STAAU   8					gp:SCH17_7	orf:25:4444Y					prf.2403350A	pir.A55225			gp:SC1A2_16	
	ORF	(dq)	474	156	324	312	2355	853	378	465	264	111	702	225	2166	273	6507	1069	1074	1521	717	1818	186
45	Terminal	(nt)	1861225	1861475	1861519	1862399	1865299	1865822	1866219	1866792	:867095	186783	1868587	1868671	1868927	1871101	1871380	1879400	1880485	1882470	1884220	1887047	1887590
<b>50</b>	ınıtıal	(nt)	1850752	1861320	1861842	1862088	5445 1862945	1865265	1865842	1856328	1856832	1867098	5451 1867886	1868895	1871092	1871373	1877886	1878312	1879412	1883990	1884936	1885230	1887405
ة مسر	SEO		5441	5442	5443	5444		5446	5447	5448	5449	5450	5451	5452	5453	5454	5455	5456	5457	5458	5459	5460	5461
55	SEO	(DNA)	1941	1942	1943	1944	1945	1945	1947	1948	1949	1950	1951	1952	1953	1954	1955	1955	1957	1958	1959	1963	1961

							Г			1								<u> </u>	Γ		Τ_	Τ		Т	Γ	Γ-	
5			tion	sse-related							ATP-binding							aratus protein									
10	•		Function	SNF2/Rad54 helicase-related protein	hypothetical protein		hypothetical protein				endopeptidase Clp ATP-binding chain B							nuclear mitotic apparatus protein									
15			Ma:ched length (a a)	06	163		537				724							1004									
20			Similarity (%)	0.07	56.4		47.9				52.5							49.1									
			Identity (%)	46.7	33.1		20.7				25.3							20.1									
25				·	·											·		-				ĺ			·		
30		Table 1 (continued)	Homologous gene	radiodurans	Lactobacillus phage phi-gle Rorf232		acis pXO2-16				oli cip3							numA									
		Table	Homol	Deinococcus radiodurans DR1258	Lactobacillus Rorf232		Bacillus anthracis pXO2-16				Escherichia coll clp3							Homo sapiens numA				-					
<i>35</i> 40			db Match	gp:AE001973_4	pir.T;3226		gp:AF188935_16				sp:CLPB_ECOLI							2766 pir.S23647									
				gb:			99											pir								_	
			ORF (bp)	351	864	330	1680	1206	1293	2493	1785	621	1113	846	981	879	198	2766	009	1251	969	714	1008	1659	1488	339	1506
45			Terminal (nt)	1887688	1888231	1889859	1892028	1891832	1893388	1894739	1897374	1899233	1899804	1901066	1902955	1902005	1903225	1903113	1905973	1906664	1907965	1908785	1909501	1910642	1912333	1913973	1914725
50			Initial (nt)	1898038	1889094	5464 1889530	5465 1891707	1893037	5467 1894680	1897231	1899158		1900916	1901911	1901975	1902883	1903028	1905878	1906572	1907914	1908660	5480 . 1909498	5481, 1910508	1912300	1913820	1914371	1916233
			SEQ NO (a a )	5462	5463	5464	5465	5456	5467	5468	5469	5470	5471	5472	5473	5474	5475	5476	5477	5478	5479	5480	5481	5482	5483	5484	5485
55		į	SEQ NO (DNA)	1962	1963	1964	1965		1967		1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980		1982	1983	1984   5484	.685

EP 1 108 790 A2

											-			7				T		T	$\prod$				
5																									
	Function										mucin			vlase					in			ië.			
10	J.T.										submaxillary apomucin			modification methylase					hypothetical protein			hypothetical protein		1	
											maxilla			dification					othetic			othetic			
	e	+	-	-	-	-	$\perp$	<del> </del>		-	<del></del>	-	-	Ę	-	+-	-	<u> </u>	a A	<u> </u>	-	hyp	-	-	
15	Matched length										1408			2					411			328			
	Similarity (%)										49.2		-	65.6			-		58.8	-		54.6		†-	
20		+	+-	-	-	-	-	H	-	-	$\vdash$	+	<del> </del>	╀	+	-	<del> </del>			-			-	$\perp$	$\sqcup$
	Identity (%)				L	<u> </u>					23.2			42.6			L.		38.6			27.1			
25 Q																			is			-			
so so so so so so so so so so so so so s	Homologous gene									 	8			<u>چ</u>					erculos			naschii			
30 el 1 (c	ologor				1						omest			coli ec				   	um tub 156			cus jan			
Ta.	Hon										Sus scrofa domestica		, 	Escherichia coli ecoR1					Mycobacterium tuberculosis H37Rv Rv1956			Methanococcus jannaschii MJ0137			
<i>35</i>		1	-			<u> </u>	ļ	_		<u> </u>	Sus			Esch	_				Myco H37F			Meth MJ01	L		
	Ę												l İ	ECOLI								ET.JA			
	db Match										pir. T03099								pir.H70638	! !		sp:Y137_METJA			
40		-	_	 	5		ക				pir T			sp:MTE1	ļ 				Pir.H.			sp:Y1			
	ORF (bp)	360		312		75	54	930	900	1 1	4464	1	945	171	375	1821	50,	468	381	203	837	942	624	210	534
45	Terminal (nt)	916733	1917165	1917329	1917564	1918703	1919646	1920347	1925695	1926038	1921547	1926259	1927245	1928381	1928908	1929059	1930990	1931421	193;935	1932373	1933522	1934971	1936849	1937202   1937411	1937485
	<b> </b>												i											72   19	
50	Initial (nt)	1916374	1916944	1917640	1918208	1919461	1920194	1921276	1925390	1925682	1926010	1926837	1928189	5498 1928211	1928534	5530 1930879	1931190	1931888	2003 :5503 1932315	1932879	1934358	1935912	1936226	19372	1938C19
	SEQ NO (a.a.)	5486	5487	5488	5485	5490	5491	5492	5493	5494	5495	5496	5497	8679	5499	5530	5501		5503	5504	5505	5506	5507	5508	5509
55	SEQ NO (DNA)	1986	1987	1988	1939	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2300	2001	2002   5502	2003	2004	2005	2006	2007	2008	2009

5		Function										surface protein				major secreted protein PS1 protein precursor			DNA topo.somerase III					major secreted protein PS1 protein precursor	
15		Matched length (a.a.)										304				270			597					344	
20		Similarity (%)										44 1				54.4			50.9					54.7	
		Identity (%)										23.0				30.7			23.8					29.7	
25	Table 1 (continued)	Homologous gene										ecalis esp				n glutamicum flavum) ATCC			lop8					n glutamicum flavum) ATCC	
30	Table	Homolo										Enterococcus faecalis esp		     		Corynebacterium glutamicum (Brevibacterium flavum) ATCC 17965 csp1			Escherichia coli top8					Corynebacterium glutamicum (Brevibacterium flavum) ATCC 17965 csp1	
35 40		db Match										prf:2509434A	i			sp.CSP1_CORGL			sp:TOP3_ECOLI					1887 sp.CSP1_CORGL	
		ORF (ap)	1191	534	588	444	753	303	216	309	985	828 p	297	381	429	1581	2430	967	2277 sı	2085	891	432	744	1887 sp	291
45		Terminal (n:)	1940135	1938531	1940844	1941550	1941732	1942812	1943310	1943653	1944564	1944608	1945595	1945952	1946609	1947070	1949021	1951619	1952546	1956203	.958450	1959765	1960371	1961114	1963139
50		ritial (nt)	1936945	1939064	1940257	1941107	1942484	1942510	1943095	1943345	1943680	1945435	1945891	1946332	5522 1947037	5523 1948550	1951450	1952495	5526 1954922	2027 5527 1958287	2028 5528 195934C	5529 1960196	5530 1961114	5531 1963000	1963429
		SEQ NC.	5510	5511	5512		5514	5515	5516	5517	5518	5519	5520	2021 5521	5522		5524	5525	5526	5527	5528		5530		5532
55		SEQ NO (DNA)	2010	2011	2012	2013	2014	20.2	20:6	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032

EP 1 108 790 A2

. 5	Function				se										single stranded DNA-binding protein								9					
10					thermonuclease										single strander	,							serine professe				-	
15	Matched length				227		1								225								249					
20	Similarity (%)				57.7						ļ 				59.1								52.6					
	Identity (%)				30.4					<u>.</u>					24.9			-	ļ		_		25.7					
25 (panuju	gene	-			one sne																		AgSP24D					
& Table 1 (continued)	Hamclogous gene				Staphylococcus aureus nuc										Shewanella sp. ssb								Ancpheles gambiae AgSP24D					
35	db Match			<del>  -</del>	4 SP.NUC_STAAU S			•							prf.23133478 S								SP.S24D ANOGA A					
40		8	76		4 Sp.N.	7	4		6	1.	6	-	9	2	4 prf.23	co.	2	7	8		60	0	2 sp.S2	3	3	7		
45	_ 5 €	514 1230	Ξ.	111 35	99	-	167 564	15 1452		174 1221	_	37 591		503 237		94 576	183 462	49 507	129   588		117 558	57	9	69	36	74	12 180	
	Terminal (nt)	3 7963514	1964727	1965911	1966964	1967269	1968167	1969715	1570203	1971474	1973(	1973737	19742	1974	1975794	1976494	1976983	1977549	1978329	1978721	1979217	1979809	1980885	1381657	1982028	1982817	1981912	
50	initial (nt)	1964743	5534 1965902	5535 1966267	5536 1966301	5537 1967435	1967604	1968264	5540 1969745	5541 1970254	197-672 1973090	1973:47	1973809: 1974204	:974267 1974503	1975-71	1975916	1976522	1977043	1977742	1978389	5552 1978660	1979239	1979974	1980965	1981663	1982071	1982091	
	SEQ NO (a.a.)	2033 5533		·i		5537	_ 1	5539	5540	5541	5542	5543	5544	5545	5546	5547	5548	5549	5550	5551	5552	5553	5554	5555	5556	5557		
55	SEQ NO:	2033	2034	2035	2036	2037	2039	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049.	2050	2051	2052	2053	2054	2055	2056	2057	2050	

BYIGULA: >ED ++10320044 1

5	Function								ıntegrase	transposase (divided)	(ransposase (divided)		fransposition repressor	insertion element (IS3 related)	transposase					major secreted protein PS1 protein precursor	ntegrase
15	Vatched lergth (aa)	:							406	124	117		31	٤7	270					153	223
20	Simi arity (%)				-				55.9	94.4	84.6		8.96	88.4	537					37.0	56.1
	Identity (%)								29.6	83.9	6.07		80.7	74.4	31.1					25.0	28.7
25 (panujuu	gene				-				ge L5 int	ofermentum	ofermentum		ofermentum	utamicum	color A3(2)					utamicum rum) ATCC	ge L5 int
Se Se Se Se Se Se Se Se Se Se Se Se Se S	Homo!agaus gene					-			Mycobacterium phage L5 int	Brevibacterium lactofermentum CGL2005 ISaB1	Brevibacterium lactofermentum CGL 2005 ISaB 1		Brevibacterium lactofermentum CGL 2005 ISaB1	Corynebacterium glutamicum orf 1	Streptomyces coelicolor A3(2) SCJ11,12					Corynebacterium glutamicum (Brevibacterium flavum) ATCC 17965 csp1	Mycobacterium phage L5 int
<i>35</i>	db Match								Sp.V'NT_BPML5	gsp:R23011	gsp:R23011		gsp:R21601	pir.S60889	gp:SCJ11_12					sp:CSP1_CORGL	Sp:VINT_BPML5
	ORF (bo)	363	273	264	234	342	273	303	1149	380	417	207	114	135	828	354	891	432	744	1584	687
45	Terminal (nt)	1983548	1983883	1984181	1984450	1984728	1985354	1985071	1985442	1987507	1987887	1988589	1988370	1988530	1988778	1991020	1989874	1991189	1991795	1992538	1954608
50	Initial (rt)	1983185	1983611	1983918	1984217	1984387	1985092	1985373	198659C	1987866	5	1986383	5570 1988483	2071 5571 1988664	1985605	1990667	1990764	1991620	1992538	2077 5577 1994121	1995294
	SEQ NO (a a.)	5559	2560	5561	5562	5563	5564	5955	5566	5567	5568	5569		5571	5225	5573	5574	5575	5576	5577	5578
55	SEQ NO (DNA)	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078

EP 1 108 790 A2

	_																,			<del></del> ,
5		د	ınsporter				s protein	ıroteın	reductase					-phosphate	se			sphate		
10		Function	sodium-dependent transporter	hypothetical protein			riboflavin biosynthesis protein	potential membrane protein	methionine sulfoxide reductase		hypothetical protein	hypothetical protein	ribonuclease D	1-deoxy-D-xylulose-5-phosphate synthase	RNA methyltransferase		hypothetical protein	deoxyuridine 5'-triphosphate nucleotidohydrolase	hypothetical protein	
15		Matched length (a.a.)	88	92			233	384	126		232	201	37:	618	472		268	140	150	
20		Similarity (%)	76.1	81.5			64.4	71.9	67.5		77.2	786	528	78.5	52.3		62 7	82 1	7.07	
		Identity (%)	39.8	48.9			33.5	42.5	41.3		55.2	55.7	25.9	55.3	25.4		38.1	55.0	46.0	
25	Table 1 (conlinued)	is gene	26595	AA			oerculosis D	oerculosis	donii msrA		oerculosis	oerculosis	enzae Rd	CL 190 dxs	ma MSB8		berculosis	licolor A3(2)	berculosis	
30	Table 1 (c	Homologous gene	Hel cobacter pylori 26595 HP0214	Bacillus subtilis yxaA			Mycobacterium tuberculosis H37Rv Rv2671 ribD	Mycobacterium tuberculosis H37Rv Rv2673	Streptococcus gordonii msrA		Mycobacterium tuberculosis H37Rv Rv2676c	Mycobacterium tuberculosis H37Rv Rv2680	Haemophilus influenzae Rd KW20 H10390 rnd	Streptomyces sp. CL190 dxs	Thermotoga maritima MSB8 TM1094		Mycobacterium tuberculosis H37Rv Rv2696c	Streptomyces coelicolor A3(2) SC2E9.09 dut	Mycobacterium tuberculosis H37Rv Rv2698	
35		ء					Z 1	2 1	2		21	21								
40		db Match	pi:F64546	sp.YXAA_BACSU			pir.C70968	pir.E70968	gp: AF128264		pir:H70968	pir:C70528	sp:RND_HAEIN	gp. AB0268311	pir:E72298		pir.C70530	sp.DUT_STRCO	pir.E70530	
		03F (bp)	306	432	345	336	969	1254	408	426	969	624	1263	1908	1236	282	861	447	549	207
45		Terminal (rt)	1995783	1996537	1997112	1997503	1998240	1999542	1959949	1999707	2000521	2002112	2003334	2003402	2005452	2006979	2006777	2007738	2008798	2009062 2008876
50		initial (nt)	1996088	1996106	1995769	1997168	1997545	1998289	1999542	2000132	2001216	2001489	2002002	2005309	2006697	2006698	2007637	2008184	2006250	
		SEQ NO (a a.)	5579	5580	5581	5882	5583	5584	5585	5586	5587	5588	5589	5590	5591	5592	5593	5594	5595	2096 5596
55		SEQ NO (DNA)	2079	2080	2081	2062	2063	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096

3	
10	
15	
20	
25	
30	
35	
40	
45	
50	

	Function	sodium-dependent transporter	hypothetical protein			riboflavin biosynthesis protein	potential membrane protein	methionine sulfoxide reductase		hypothetical protein	hypothetical protein	ribonuclease D	1-deoxy-D-xylulose-5-phosphate synthase	RNA methyltransferase		hypothetical protein	deoxyuridine 5'-triphosphate nucleotidohydrolase	hypothetical protein	
	Matched length (a.a.)	88	95			233	384	126		232	201	371	618	472		268	140	150	
	Similarity (%)	76.1	81.5			64.4	71.9	67.5		77.2	78.6	52.8	78.5	52.3		62.7	82.1	7.07	
	Identity (%)	39.8	48.9			33.5	42.5	41.3		55.2	55.7	25.9	55.3	25.4		38.1	55.0	46.0	
Table 1 (continued)	Homologous gene	Helicobacter pylori 26695 HP0214	Bacillus subtilis yxaA			Mycobacterium tuberculosis H37Rv Rv2671 ribD	Mycobacterium tuberculosis H37Rv Rv2673	Streptococcus gordonii msrA	-	Mycobacterium tuberculosis H37Rv Rv2676c	Mycobacterium tuberculosis H37Rv Rv2680	Haemophilus influenzae Rd KW20 H10390 rnd	Streptomyces sp. CL190 dxs	Thermotoga maritima MSB8 TM1094		Mycobacterium tuberculosis H37Rv Rv2696c	Streptomyces coelicolor A3(2) SC2E9.09 dut	Mycobacterium tuberculosis H37Rv_Rv2698	
	db Match	pir.F64546	sp:YXAA_BACSU	,		pir.C70968	pir:E70968	gp:AF128264_2		pir:H70968	pir.C70528	sp.RND_HAEIN	gp.AB026631_1	pir.E72298		pir.C70530	sp.DUT_STRCO	pir:E70530	
	ORF (bp)	306	432	345	336	969	1254	408	426	969	624	1263	1908	1236	282	861	447	549	207
	Terminal (nt)	1995783	1996537	1997112	1997503	1998240	1999542	1999949	1999707	2000521	2002112	2003334	2003402	2005462	2006979	2006777	2007738	2008798	2008876
	Initial (nt)	1996088	1996106	1996768	1997168	1997545	1998289	1999542	2000132	2001216	2001489	2002002	2005309	2006697	2006698	2007637	2008184	2008250	20090082
	SEQ NO	5579	5580	5581	5582	5583	5584	5585	5586	5587	5588	5589	5590	5591	5592	5593	5594	5595	9659
	SEQ NO (DNA)	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2082	2093	2094	2095	2096

	Function	hypothetical protein	extragenic suppressor protein	polyphosphate glucokinase	sigma factor or RNA polymerase transcription factor	hypothetical membrane protein		hypothetical protein	hypothetical membrane protein	hypothetical protein	transferase	hypothetical protein.	iron dependent repressor or diphtheria toxin repressor	putative sporulation protein	UDP-glucose 4-epimerase	***************************************	hypothetical protein	ATP-dependent RNA helicase
	Matched length (a.a.)	100	198	248	200	422		578	127	9/	523	144	22 <sup>8</sup>	77	329		305	661
	Similarity (%)	81.0	68.2	80.2	98.6	51.4		808	59.1	85.5	61.2	100.0	9.66	64.0	99.1		79.0	50.7
	tdentity (%)	58.0	38.4	54.4	98.0	23.9		61.3	32.3	65.8	33.5	97.2	98.7	62.0	99.1		45.3	24.4
Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv2699c	Escherichia coli K12 suhB	Mycobacterium tuberculosis H37Rv RV2702 ppgK	Corynebacterium glutamicum sigA	Bacillus subtilis yrkO		Mycobacterium tuberculosis H37Rv Rv2917	Mycobacterium tuberculosis H37Rv Rv2709	Mycobacterium tuberculosis H37Rv Rv2708c	Streptomyces coelicolor A3(2) SCH5.08c	Corynebacterium glutamicum ATCC 13869 ORF1	Corynebacterium glutamicum ATCC 13869 db:R	Streptomyces aureofaciens	Corynebacterium glutamicum ATCC 13869 (Brevibacterium lactofermentum) galE		Mycobacterium tuberculosis H37Rv Rv2714	Saccharomyces cerevisiae YJL050W dob1
	db Match	pir:F70530	sp.SUHB_ECOLI	sp:PPGK_MYCTU	prf.2204286A	sp.YRKO_BACSU		sp:Y065_MYCTU	pir:H70531	pir.G70531	gp:SCH5_8	prf:2204286C	pir:140339	GP:AF010134_1	sp.GALE_BRELA		pir.E70532	2550 sp:MTR4_YEAST
	ORF (bp)	291	816	828	1494	1335	537	1710	636	237	1533	432	684	234	987	1323	957	2550
	Terminal (nt)	2009280	2009724	2011382	2013356	2014162	2015585	2016257	2018754	2017966	2020276	2020724	2022949	2022313	2023945	2023948	2026379	2029043
	Initial (nt)	2009570	2010539	2010555	2011863	2015496	2016121	2017966	2018119	2018202	2018744	2020293	2022266	2022546	2022959	2025270	2025423	2026494
	SEQ NO.	5597	5598	5599	2600	5601	5602	5603	5604	5095	9099	5607	5608	9095	5610	5611	5612	5613
	SEQ NO (DNA)	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113

Table 1 (continued)

_																				
	Function	hydrogen peroxide-inducible genes activator		ATP-dependent helicase	regulatory protein		SOS regulatory protein	galactitol utilization operon repressor	phosphofructokinase (fructose 1- phosphate kinase)	phosphoenolpyruvate-protein phosphotransferase	glycerol-3-phosphate regulon repressor	1-phosphofructokinase or 6- phosphofructokinase	PTS system, fructose-specific IIBC component	phosphocarrier protein		uracil permease	ATP/GTP-binding protein			diaminopimelate epimerase
	Matched length (a.a.)	299		1298	145		222	245	320	592	262	345	549	81		407	419			269
	Similarity (%)	65.6		76.2	86.2		71.6	67.8	55.6	64.0	62.6	55.7	9'69	71.6		70.5	0.08			64.7
į	identity (%)	35.8		49.2	61.4		46.9	33 9	27.2	34.3	26.7	33.0	43.0	37.0		39.1	54.4			33.5
Table 1 (continued)	Homologous gene	Escherichia coli oxyR		Escherichia coli hrpA	Streptomyces clavuligerus nrdR		Bacillus subtilis dinR	Escherichia coli K12 gatR	Streptomyces coelicolor A3(2) SCE22.14c	Bacillus stearothermophilus ptsl	Escherichia coli K12 glpR	Rhodobacter capsulatus fruK	Escherichia coli K12 fruA	Bacillus stearothermophilus XL- 65-6 ptsH		Bacillus caldolyticus pyrP	Streptomyces fradiae orf11*			Haemophilus influenzae Rd KW20 H10750 dapF
	db Match	sp OXYR_ECOLI		sp.HRPA_ECOLI	gp:SCAJ4870_3		sp.LEXA_BACSU	sp:GATR_ECOLI	gp.SCE22_14	sp.PT1_BACST	sp:GLPR_ECOLI	sp:K1PF_RHOCA	sp:PTFB_ECOLI	sp. PTHP_BACST		Sp:PYRP_BACCL	gp. AF145049_8			sp.DAPF_HAEIN
	ORF (bp)	981	1089	3906	450	420	969	777	096	1704	792	066	1836	267	582	1287	1458	786	537	831
-	Terminal (nt)	2030157	2030277	2035383	2035431	2035990	2037507	2038591	2039550	2039618	2042519	2043508	2045571	2046028	2046714	2047320	2048650	2051106	2051842	2051845
	Initial (nt)	2029177	2031365	2031478	2035880	2036409	2036812	2037815	2038591	2041321	2041728	2042519	2043736	2045762	2047295	2048606	2050107	2050321	2051306	5632 2052675
	SEQ NO (a a)	5614	5615	5616	5617	5618	5619	5620	5621	5622	5623	5624	5625	5626	5627	5628	5629	5630	5631	5632
	SEQ NO (DNA)	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132

Function	tRNA detta-2- isopentenylpyrophosphate transferase		hypothetical protein			hypothetical membrane protein	hypothetical protein	glulamate transport ATP-binding protein	Neisserial nolynentides predicted to Neisserial polypeptides predicted to be useful antigens for vaccines and diagnostics	glutamate transport system permease protein	glutamate transport system permease protein	regulatory protein	hypothetical protein		biotin synthase	putrescine transport ATP-binding protein	hypothetical membrane protein
Matched length (a a)	300		445			190	494	242	71	225	273	142	29		197	223	228
Simitarity (%)	68.7		757			63.7	86.4	9 66	73.0	100 0	9.66	6.99	71.6		61.4	69.5	588
Identity. (%)	40.0		48.5			29.0	68.4	99.6	0.99	100.0	99.3	34.5	40.3		33.0	33.2	24.6
Homologous gene	Escherichia coli K12 miaA		Mycobacterium tuberculosis H37Rv Rv2731			Mycobacterium tuberculosis H37Rv Rv2732c	Mycobacterium leprae B2235_C2_195	Corynebacterium glutamicum ATCC 13032 gluA	Neisseria gonorrhoeae	Corynebacterium glutamicum ATCC 13032 gluC	Corynebacterium glutamicum (Brevibacterium flavum) ATCC 13032 gluD	Mycobacterium leprae recX	Mycobacterium tuberculosis H37Rv Rv2738c		Bacillus sphaericus bioY	Escherichia coli K12 potG	Bacillus subtilis ybaF
db Match	sp:MIAA_ECOL!		pir:B70506			pir:C70506	sp:Y195_MYCLE	sp:GLUA_CORGL	GSP: Y75358	sp.GLUC_CORGL	sp:GLUD_CORGL	sp:RECX_MYCLE	pir.A70878		Sp.BIOY_BACSH	sp:POTG_ECOLI	pir.F69742
ORF (bp)	903	675	1359	1020	1023	699	1566	726	219	684	819	597	234	738	576	669	609
Terminal (nt)	2052684	2053609	2055761	2054724	2056787	2057120	2057855	2060499	2060196	2062312	2063259	2063298	2065394	2065667	2067141	2067866	2068474
Initial (nt)	2053586	2054283	2054403	2055743	2055765	2057788	2059420	2059774	2060414	2061629	2062441	2063894	2065627	2066404	2066566	2067168	2067866
SEQ NO (a.a.)	5633	5634	5635	5636	5637	5638	5639	5640	5641	5642	5643	5644	5645	5646	5647	5648	5649
SEQ NO. (DNA)	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149
	SEQ Initial Terminal ORF db Match Homologous gene (M) (h) (bp) (bp)	SEQ Initial (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt)	SEQ Initial (a.a.)         Terminal (bp)         GRF (bp)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)           5633         2053586         2052684         903         sp:MIAA_ECOLI         Escherichia coli K12 miaA         40.0         68.7         300           5634         2054283         2053609         675         675         675         68.7         300	SEQ Initial (nl) (nl) (nl) (nl) (nl) (nl) (nl) (nl	SEQ Initial (nt)         Terminal (nt)         ORF (pp)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)           56.33         205.3586         205.2684         90.3         sp.MIAA_ECOL1         Escherichia coli K12 miaA         40.0         68.7         300           56.34         205.4283         205.3609         67.5         mycobacterium tuberculosis         48.5         75.7         445           56.35         205.4403         205.4724         1020         1370         1020	SEQ NO (a.a.)         Initial (nt)         Terminal (nt)         ORF (bp)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matched (%)	SEQ Initial (nt)         Terminal (nt)         ORF (pp)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)           5633         2053586         2052684         903         sp.MIAA_ECOL1         Escherichia coli K12 miaA (%)         40.0         68.7         300           5634         2054283         2053609         675         AMYCObacterium tuberculosis         48.5         75.7         445           5635         2054403         2054724         1020         Mycobacterium tuberculosis         48.5         75.7         445           5637         2055761         1023         Mycobacterium tuberculosis         29.0         63.7         190           5638         2057788         2057120         669         pir.C70506         Mycobacterium tuberculosis         29.0         63.7         190	SEQ NO (a.1)         Initial (nt)         Terminal (nt)         ORF (bp)         db Match         Homologous gene         Identity (%)         Similarity (%)         Matched (%)         Matched (%)	SEQ Initial (a)         Terminal (b)         ORF (b)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)           NO (a)         (II)         (III)         (b)         Ab Match         Homologous gene (%)         (%)	SEQ (n1)         Initial (n1)         Terminal (nt)         (DR (bp))         About the Match (pp)         Homologous gene (pp)         Identity. Similarity (pp)         Matched (pp)           5633         2053586         2052684         903         sp.MIAA_ECOLI         Escherichia coli K12 miaA         40.0         68.7         300           5634         2053286         2053689         675         Mycobacterium tuberculosis         48.5         75.7         445           5635         2053743         2054724         1023         Mycobacterium tuberculosis         29.0         63.7         190           5636         2055765         2056787         1023         Mycobacterium tuberculosis         29.0         63.7         190           5638         2057766         2057120         669         pir.C70506         Mycobacterium floramicum         99.6         89.6         494           5639         205974         2060499         726         sp.Y195_MYCLE         Mycobacterium glutamicum         99.6         99.6         242           5641         2060414         2060499         726         sp.Y75358         Neisseria gonorrhoeae         66.0         73.0         71	SEO (nI) (10.1)         Initial (10.1)         Terminal (10.1)         ORF (10.1)         db Match (10.1)         Homologous gene (10.6)         Identity (10.6)         Similarity (10.6)         Matched (10.6)	SEG (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt)	SEC NO 1011 102 103 103 103 103 103 103 103 103 103 103	SEC (a.a.)         Innital (Int)         Terminal (Int)         ORF (Int)         db Match         Homologous gene         Identity (%)         Similarity (%)         Matched (%)         Matched (%) <td>SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity         Similarity (%)         Matched (%)<td>SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity (%)         Similarin (%)         Matched (%)&lt;</td><td>SEO (nitial)         Terminal (bp)         GPF (vb)         db Match         Homologous gene (vb)         (vb) (vb)         Matched (vb)</td></td>	SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity         Similarity (%)         Matched (%) <td>SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity (%)         Similarin (%)         Matched (%)&lt;</td> <td>SEO (nitial)         Terminal (bp)         GPF (vb)         db Match         Homologous gene (vb)         (vb) (vb)         Matched (vb)</td>	SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity (%)         Similarin (%)         Matched (%)<	SEO (nitial)         Terminal (bp)         GPF (vb)         db Match         Homologous gene (vb)         (vb) (vb)         Matched (vb)

Table 1 (continued)

						/				
SEQ NO.	SEQ NO (a a.)	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched length (a a)	Function
2150	5650	2068703	2069392	069	pir.B60176	Mycobacterium tuberculosis	41.7	78.5	228	hypothetical protein
2151	5651	2069383	2068556	828	sp.35KD_MYCTU	Mycobacterium tuberculosis H37Rv RV2744C	72.5	9.69	269	hypothetical protein (35kD protein)
2152	5652	2069936	2069616	321	pir:H70878	Mycobacterium tuberculosis H37Rv Rv2745c	54.2	78.3	83	regulator (DNA-binding protein)
2153	5653	2070512	2069997	516	sp.CINA_STRPN	Streptococcus pneumoniae R6X cinA	41.8	68.5	165	competence damage induced proteins
2154	5654	2071121	2070519	603	prf.2421334D	Streptococcus pyagenes pgsA	38.8	72.5	160	phosphotidylglycerophosphate synthase
2155	5655	2071315	2071599	285	pir:T10688	Arabidopsis thaliana ATSP T16118.20	24.8	52.1	117	hypothetical protein
2156	5656	2071624	2071740	117	gp.AF071810_1	Streptococcus pneumoniae DBL5 pspA	0.09	70 0	30	surface protein (Peumococcal surface protein A)
2157	5657	2072066	2072878	813		,				
2158	5658 5658	2072905	2071799	1187	p.f. 2118285B	Escherichia coli terG	31.0	59.8 59.8	358	tellurite resistance protein
2159	5659	2076056	2073294	2763	sp.SP3E_BACSU	Bacillus subtilis 168 spottlE	38.0	64.6	845	stage III sporulation protein E
2160	5660	2077024	2076392	633	gp:SC4G6_14	Streptomyces coelicolor A3(2) SC4G6.14	33.3	610	216	hypothetical protein
2161	5661	2079275	2077122	2154	sp.YOR4_CORGL	Corynebacterium glutamicum ATCC 13032 orf4	99.1	99 4	645	hypothetical protein
2162	5662	2081136	2080387	750	sp.YOAP_BRELA	Corynebacterium glutamicum (Brevibacterium lactofermentum) ATCC 13869 orf2	99.2	9.66	250	hypothetical protein
2163	5663	2082115	2082813	669						
2164	5664	2082368	2082105	264						
2165	5995	2085190	2082932	2259	prf.2217311A	Streptomyces antibioticus gpsl	65.4	85 3	742	guanosine pentaphosphate synthetase
2166	9999	2085702	2085436	267	pir:F69700	Bacillus subtilis rpsO	64.0	88.8	89	30S ribosomal protein S15
2167	2995	5667 2086826	2085879	948	prf.2518365A	Leishmania major	35.1	63 3	319	nucleoside hydrolase

Table 1 (continued)

	Function	bifunctional protein (riboflavin kinase and FAD synthetase)	tRNA pseudouridine synthase B	hypothetical protein	hypothetical protein	phosphoesterase	DNA damaged inducible protein f	hypothetical protein	ribosome-binding factor A	translation initiation factor IF-2	hypothetical protein	n-utilization substance protein (transcriptional termination/antitermination factor)		hypothetical protein	peptide-binding protein	peptidetransport system permease	oligopeptide permease	peplidetransport system ABC- transporter ATP-binding protein
	Matched length (a a)	329 bi	303 tF	47 h	237 hy	273 pl	433 D	308	108 ri	1103 tr	83 h	352 (t		165 h	534 p	337 р	292 0	552 P
	Similarity (%)	79.0	61.7	73.0	62.5	68.9	78.8	70.8	70.4	62.9	66.3	71.0		65.5	6.09	69.4	69.2	81.3
	identity (%)	56.2	32.7	65.0	42.2	46.9	51.0	36.7	32.4	37.7	44.6	42.3		34.6	25.3	37.7	38.4	57.6
lable I (collillinged)	Homologous gene	Corynebacterium ammoniagenes ATCC 6872 ribF	Bacillus subtilis 168 truB	Corynebacterium ammoniagenes	Streptomyces coelicolor A3(2) SC5A7.23	Mycobacterium tuberculosis H37Rv Rv2795c	Mycobacterium tuberculosis H37Rv Rv2836c dinF	Mycobacterium tuberculosis H37Rv RV2837c	Bacillus subtilis 168 rbfA	Stigmatella aurantiaca DW4 infB	Streptomyces coelicolor A3(2) SC5H4.29	Bacillus subtilis 168 nusA		Mycobacterium tuberculosis H37Rv Rv2842c	Bacillus subtilis 168 dppE	Escherichia coli K12 dppB	Bacillus subtilis spo0KC	Mycobacterium tuberculosis H37Rv Rv3663c dppD
	db Match	sp.RIBF_CORAM	sp.TRUB_BACSU	PIR:PC4007	gp:SC5A7_23	pir.B70885	pir.G70693	pir:H70693	sp.RBFA_BACSU	sp:IF2_STIAU	gp:SC5H4_29	sp.NUSA_BACSU		pir.E70588	sp.DPPE_BACSU	sp.DPPB_ECOLI	prf:1709239C	31 pir.H70788
	ORF (bp)	1023	891	228	651	804	1305	966	447	3012	336	966	1254	534	1602	924	666	1731
	Terminal (nt)	2086919	2088863	2087954	2089218	2089861	2090751	2092051	2093055	2093712	2096844	2097380	2099815	2098412	2101841	2102946	2103973	2105703
	Initial (nt)	2087941	2087973	2088181	2089868	2090664	2092055	2093046	2093501	2096723	2097179	2098375	2098562	2098945	2100240	2102023	2102975	2103973
	SEQ NO		5669	5670	5671	5672	5673	5674	5675	5676	5677	5678	5679	5680	5681	5682	5683	5684
	SEQ NO.	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184

response regulator (two-component hypothetical membrane protein two-component system sensor histidine kinase magnesium-chelatase subunit magnesium-chelatase subunit 5 methionine aminopeptidase system response regulator) penicillin binding protein prolyl-tRNA synthetase Function glutathione reductase uroporphyrinogen III methyltransferase hypothetical protein hypothetical protein hypothetical protein hypothetical protein 10 15 Matched length 252 630 216 424 360 (a.a) 338 466 243 342 488 237 151 37 Similarity 56.5 56.8 84.6 65.0 9.69 738 68.7 65.7 9.97 75.8 72.2 60.7 8 58 62 20 Identity (%) 46.5 53.0 47.2 27.3 44.0 29.5 24.4 0.79 49.0 41.2 Θ 35.1 32. 39 37 Rhodobacter sphaeroides ATCC 17023 bchD Streptomyces clavuligerus pcbR Propionibacterium freudenreichii cobA 25 Streptomyces coelicolor A3(2) SC5H1.10c Burkholderia cepacia AC1100 gor Streptomyces coelicolor A3(2) SCC30.05 Clostridium perfringens NCIB 10662 ORF2 Corynebacterium diphtheriae chrA Corynebacterium diphtheriae chrS Table 1 (continued) Mycobacterium tuberculosis H37Rv Rv2854 Mycobacterium tuberculosis H37Rv Rv2845c proS Deinococcus radiodurans DRA0279 Escherichia coli K12 map Homologous gene Heliobacillus mobilis bchl 30 35 sp.BCHD\_RHOSH Sp.GSHR\_BURCE SP. AMPM\_ECOLI gp: AE001863\_70 sp:YPLC\_CLOPE SP:SYP\_MYCTU prf.2503462AA gp:SC5H1\_10 prf.2518330B prf.2518330A db Match prt 2224268A prf.2108318B gp:SCC30\_5 pir:A70590 40 789 1866 1149 1014 1395 1422 1764 1101 729 630 957 759 942 유 (명) 735 750 900 357 2119080 2121296 2110434 2116774 2118310 2117015 2119495 2120356 2120359 2123219 2123848 2126045 2112659 Terminal (nt) 2109155 2112717 45 2105801 2108386 2108389 2119139 2121147 2123161 5702 2125089 2123848 2111238 2113616 5693 2116916 2117956 2118607 2119628 2124996 2107564 2110255 2115761 2109147 2111183 2107652 Initial Ę 50 5695 5694 5695 5696 5697 5698 5699 5700 5701 5691 5685 5686 5687 5688 5689 5690 SEQ NO (a.a) 2193 2195 2198 2200 (DNA) 2192 2194 2196 2197 2199 2190 2186 2187 2188 2191 9 55

,	
5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

						Tabte 1 (continued)				
SEQ NO	O SEO NO. NO.	O Initial	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched length (a.a.)	Function
22	<del>-</del>	13 2126064	2126753	069	prf 2420410P	Bacillus subtilis 168 yvrO	37.3	711	225	ABC transporter
22	2204 5704	2127087	2126926	162						
22	-		2127350	1134	sp.GCPE_ECOLI	Escherichia coli K12 gcpE	44.3	73.8	359	hypothetical protein (gcpE protein)
22	2206 5706	36 2128850	2129461	612						
22	2207 5707	77 2129880	2128669	1212	pir.G70886	Mycobacterium tuberculosis H37Rv Rv2869c	43.0	736	405	hypothetical membrane protein
22	2208 5708	2130306	2130950	645	GSP:Y37145	Chlamydia trachomatis	36.0	43.0	147	polypeptides can be used as vaccines against Chlamydia trachomatis
22	2209 5709	09 2131078	2129903	1176	sp.DXR_ECOLI	Escherichia coli K12 dxr	22.8	42.0	312	1-deoxy-D-xylulose-5-phosphate reductoisomerase
22	2210 5710	10 2131322	2131762	441						
22	2211 5711	11 2131726	2131247	480						
75	2212 5712	12 2133402	2131825	1578						
22				855	pir.B72334	Thermotoga maritima MSB8 TM0793	37.1	75 1	245	ABC transporter ATP-binding protein
72	2214 5714	14 2135551	2134454	1098	sp:YS80_MYCTU	Mycobacterium tuberculosis H37Rv	66.0	780	356	pyruvate formate-iyase 1 activating enzyme
22	2215 5715	15 2135884	2136141	258	pir.A70801	Mycobacterium tuberculosis H37Rv Rv3760	41.5	74.5	94	hypothetical membrane protein
22	2216 5716	16 2137089	2136235	855	sp.CDSA_PSEAE	Pseudomonas aeruginosa ATCC 15692 cdsA	33.3	56.5	294	phosphatidate cylidylyltransferase
72	2217 5717	17 2137840	2137286	555	sp.RRF_BACSU	Bacillus subtilis 168 frr	47.0	843	185	ribosome recycling factor
72	2218 5718	18 2138664	2137936	729	prf.2510355C	Pseudomonas aeruginosa pyrH	28.4	43.1	109	uridylate kinase
22	2219 5719	19 2138994	2139854	861						
	2220 5720	20 2139827	2139003	825	sp.EFTS_STRCO	Streptomyces coelicolor A3(2) SC2E1.42 tsf	49.6	76.8	280	elongation factor Ts
22	2221 5721	21 2140886	2140071	816	pir. A69699	Bacillus subtilis rpsB	54.7	83 5	254	30S ribosomal protein S2

Table 1 (continued)

	Function	hypothetical protein	site-specific recombinase	hypothetical protein	Mg(2+) chelatase family protein	hypothetical protein	hypothetical protein	ribonuclease Hil		signal peptidase	Fe-regulated protein		50S ribosomal protein L19	thiamine phosphate pyrophosphorylase	oxidoreductase	thiamine biosynthetic enzyme thiS (thiG1) protein	thiamine biosynthetic enzyme thiG protein	molybdopterin biosynthesis protein
	Matched length (a.a.)	120	297	395	504	119	101	190		285	323		111	225	376	62	251	437
	Similarity (%)	58.0	68.7	668	75.8	72.3	96.0	69.5		61.1	59.1		88.3	6.09	64.1	74.2	76.9	56.8
	Identity (%)	46.0	40.1	39.8	46.6	40.3	68.3	42.6		32.3	25.4		70.3	28.4	34.0	37.1	48.2	30.2
ומחוב ו (בסוווווומבת)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv2891	Proteus mirabilis xerD	Mycobacterium tuberculosis H37Rv Rv2896c	Mycobacterium tuberculosis H37Rv Rv2897c	Mycobacterium tuberculosis H37Rv Rv2898c	Mycobacterium tuberculosis H37Rv Rv2901c	Haemophilus influenzae Rd H11059 rnhB	-	Streptomyces lividans TK21 sipY	Staphylococcus aureus sirA		Bacillus stearothermophilus rplS	Bacillus subtilis 168 thiE	Streptomyces coelicolor A3(2) SC6E10.01	Escherichia coli K12 thiS	Escherichia coli K12 thiG	Emericella nidulans cnxF
	db Match	sp:YS91_MYCTU	prf.2417318A	sp:YX27_MYCTU	sp:YX28_MYCTU	sp.YX29_MYCTU	sp:YT01_MYCTU	sp.RNH2_HAEIN		prt.2514288H	prf.2510361A		sp:RL19_BACST	sp.THIE_BACSU	gp:SC6E10_1	sp THIS_ECOLI	sp:THIG_ECOL!	prf 2417383A
	ORF (bp)	504	924	1182	1521	366	303	627	792	786	936	213	339	663	1080	195	780	1134
	Terminal (nt)	2141760	2141763	2142885	2144066	2145576	2146264	2146566	2148022	2147261	2149166	2149359	2149634	2150997	2152118	2152329	2153113	2154191
	Initial (nt)	2141257	2142686	2144066	2145586	5726 2145941	2146566	2147192	2147231	2148046	2148231	2149571	2149972	2150335	2151039	2152135	2152334	2238 5738 2153058
	SEQ NO (a a.)	5722	5723	5724	5725		5727	5728	5729	5730	5731	5732	5733	5734	5735	5736	5737	5738
	SEQ NO (DNA)	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238

	5	
	10	
•	15	
	20	
	25	
	30	
	35	
	40	
	45	
	50	

	Function	transcriptional accessory protein	sporulation-specific degradation regulator protein	dicarboxylase translocator	2-oxoglutarate/malate translocator	3-carboxy-cis, cis-muconate cycloisomerase				tRNA (guanine-N1)- methyltransferase	hypothetical protein	16S rRNA processing protein	hypothetical protein	30S ribosomal protein S16	inversin	ABC transporter	ABC transporter	signal recognition particle protein				cell division protein
	Matched length (a a)	776	334	456	99	350				273	210	172	69	83	196	256	318	559				505
	Similarity (%)	78.7	65.3	78.3	80.0	€ 99				64.8	97.6	72.1	2 99	79.5	61.7	69.1	63.8	78.2				66.1
	Identity (%)	9.95	27.0	45.8	40.0	39.1	-			34.8	30.5	52.3	29.0	47.0	32.1	26.6	35.5	58.7				37.0
Table 1 (continued)	Homologous gene	Bordetella pertussis TOHAMA I tex	Bacillus subtilis 168 degA	Chlamydophila pneumoniae CWL029 ybhl	Spinacia oleracea chloroplast	Pseudomonas putida pcaB				Escherichia coli K12 trmD	Stratomyces coelicolor A3(2) SCF81.27	Mycobacterium leprae MLCB250.34. rimM	Helicobacter pylori J99 jhp0839	Bacillus subtilis 168 rpsP	Mus musculus inv	Streptococcus agalactiae cylB	Pyrococcus horikoshii OT3 mtrA	Bacillus subtilis 168 ffh				Escherichia coli K12 ftsY
	db Match	sp_TEX_BORPE	pir:A36940	pir:H72105	prf 2108268A	sp:PCAB_PSEPU				sp:TRMD_ECOLI	gp:SCF81_27	SP.RIMM_MYCLE	pir:B71881	pir:C47154	pir:T14151	prf.2512328G	prt:2220349C	sp:SR54_BACSU				530 Sp.FTSY_ECOLI
	ORF (bp)	2274	975	1428	219	1251	66	393	690	819	648	513	348	495	576	867	876	1641	633	417	699	1530
	Terminal (nt)	2154460	2156747	2157754	2159019	2159287	2160768	2161111	2161507	2162196	2163745	2163748	2164737	2164815	2166098	2166124	2166990	2167944	2171058	2172131	2172877	2175288 2173759
	Initral (nt)	2156733	2157721	2159181	2159237	2160537	2160670	2161503	2162196	2163014	2163098	2164260	2164390	2165309	2165523	2166990	2167865	2169584	2170426	2171715	2172209	2175288
	SEQ NO (a a.)	5739	5740	5741	5742	5743	5744	5745	5746	5747	5748	5749	5750	5751	5752	5753	5754	5755	5756	5757	5758	5759
	SEQ NO. (DNA)	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259

hypothetical protein

6.9/

50.0

Mycobacterium tuberculosis H37Rv Rv2927c

sp:Y06G\_MYCTU

789

2190540 2193165 2194694

2191328

5775

transport protein ABC transporter

559 238

> 55.6 **58 B** 62.6

28.3 26.6 35.3

541 388

hypothetical protein

Streptomyces coelicolor A3(2) SC9C7.02

Escherichia coli K12 cydC Streptomyces verticillus

SP.CYDC\_ECOLI

1530

2193165

5777

5776 2191522

2276

gp:SC9C7\_2

441

2198007

5779 2198447

1644 prf.2104260G

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

5 .	Function			glucan 1,4-alpha-glucosidase or glucoamylase S1/S2 precursor		chromosome segregation protein	acylphosphatase		transcriptional regulator	hypothetical membrane protein			cation efflux system protein	formamidopyrimidine-DNA glycosylase	ribonuclease III	hypothetical protein
15	Matched length (a.a.)			1144		1206	92		305	257			188	285	221	176
20	Similarity (%)			46.2		72.6	73.9		0.09	73.5			9.92	2 99	76.5	62.5
	Identity (%)			22.4		48.3	51.1		23.9	39.3			46.8	36.1	40.3	35.8
25 <b>(p</b> en	đ)			ae		osis	osis		R				gep	tM or	S	osis
55 os os os os os os os os os os os os os	Homologous gene			Saccharomyces cerevisiae S288C YIR019C sta1		Mycobacterium tuberculosis H37Rv Rv2922c smc	Mycobacterium tuberculosis H37Rv RV2922 1C		Escherichia coli K12 yfeR	Mycobacterium leprae MLCL581,28c			Dichelobacter nodosus gep	Escherichia coli K12 mutM or fpg	Bacillus subtilis 168 rncS	Mycobacterium tuberculosis H37Rv Rv2926c
40	db Match			SP.AMYH_YEAST		sp:Y06B_MYCTU	sp.ACYP_MYCTU		sp.YFER_ECOLI	pir.S72748			gp:DNINTREG_3	sp:FPG_ECOLI	pir.B69693	sp.Y06F_MYCTU
	ORF (bp)	159	702	3393	963	3465	282	1854	828	831	<u>85</u>	447	615	858	741	534
45	Terminal (nt)	2175888	2177103	2176110	2181880	2179628	2183110	2183405	2185351	2187129	2187342	2187233	2187692	2188313	2189166	2189906
50	Initial (nt)	2176046	2176402	2179502	2180918	2183092	2183391	2185258	2186208	2186299	2187160	2187679	2188306	2189170	2189906	5774 2190439
	SEQ NO (a a)	2760	5761	5762	5763	5764	5765	5766	5767	5768	5769 5769	5770	5771	5772	5773	
55	SEQ NO.	2260	2261	2362	2263	2264	2265	2266	2267	2268	2269	2270	2271	2222	2273	2274

Fig. 19   Fig.	÷					$\neg$	-	T				П		Se			<u>-</u>	1	ح ⊆
Table 1 (continued)   Terminal   ORF   Abatch   Homologous game   (%)	5		noi			rotein			horylase / ylase		ılglyceryl	nosphate late synthase	rane protein	IP cyclohydrola		ohate	nimino-5- rboxamide	ınsferase	sistance proteir transport protei
Second   Comparison   Second	10		Funct	nypothetical protein	oeptidase	sucrose transport p			maltodextrin phosp glycogen phosphor	hypothetical proteir	prolipoprotein diacy transferase	indole-3-glycerol-pl synthase / anthran component II	hypothetical memb	phosphoribosyl-AN	cyclase	inositol monophos phosphatase	phosphoribosylforr aminoimidazole ca ribotide isomerase	glutamine amidotra	chloramphenicol re or transmembrane
SEC	15		Matched length (aa)										228	68	258	241	245	210	402
SEQ	20		Similarity (%)	43.7	64.3	51.9			67.4	66.4	65.5	62.1	58.8	79.8	97.7	94.0	97.6	92.4	54.0
SEQ         Initial         Terminal         ORF         db Match           (n1)         (n1)         (n1)         (pp)         db Match           (5780         2198475         2199758         1284         pir A72322           5781         2199808         2201070         1263         sp:HIPO_CAMJE           5782         2201408         2201073         336         pir.S38197           5783         2201684         2201450         135           5784         2201689         2201594         276           5785         22054591         2201592         2550         prf.S38197           5786         22054591         2201592         2550         prf.S38197           5786         22054591         2201592         2550         prf.S13410A           5786         22054591         2204591         900         sp.YFIE_BACSU           5787         2208249         2204591         901         sp.HTPG_EMENI           5788         2209167         2208367         801         sp.HTRPG_EMENI           5789         2210273         2209320         354         sp.HIS3_RHOSH           5790         2211675         2211682         738         sp.HS6CO			Identity (%)	21.0	32.9	27.1			36.1	33.9	31.4	29.6	29.4	528	97.3	94.0	95.9	2.98	25.6
SEQ         Initial         Terminal         ORF         db Match           (n1)         (n1)         (n1)         (pp)         db Match           (5780         2198475         2199758         1284         pir A72322           5781         2199808         2201070         1263         sp:HIPO_CAMJE           5782         2201408         2201073         336         pir.S38197           5783         2201684         2201450         135           5784         2201689         2201594         276           5785         22054591         2201592         2550         prf.S38197           5786         22054591         2201592         2550         prf.S38197           5786         22054591         2201592         2550         prf.S13410A           5786         22054591         2204591         900         sp.YFIE_BACSU           5787         2208249         2204591         901         sp.HTPG_EMENI           5788         2209167         2208367         801         sp.HTRPG_EMENI           5789         2210273         2209320         354         sp.HIS3_RHOSH           5790         2211675         2211682         738         sp.HS6CO	25	ed)		88	ပ္ပ	-			alP		DA 485	1	Sis	s ATCC	icum	icum	icum	icum	3 cmlR
SEQ         Initial         Terminal         ORF         db Match           (n1)         (n1)         (n1)         (pp)         db Match           (5780         2198475         2199758         1284         pir A72322           5781         2199808         2201070         1263         sp:HIPO_CAMJE           5782         2201408         2201073         336         pir.S38197           5783         2201684         2201450         135           5784         2201689         2201594         276           5785         22054591         2201592         2550         prf.S38197           5786         22054591         2201592         2550         prf.S38197           5786         22054591         2201592         2550         prf.S13410A           5786         22054591         2204591         900         sp.YFIE_BACSU           5787         2208249         2204591         901         sp.HTPG_EMENI           5788         2209167         2208367         801         sp.HTRPG_EMENI           5789         2210273         2209320         354         sp.HIS3_RHOSH           5790         2211675         2211682         738         sp.HS6CO	30	Table 1 (continu	Homologous gene	notoga maritima MS 396	pylobacter jejuni ATC 1 hipO	idopsis thaliana SUC			mococcus litoralis ma	llus subtilis 168 yfiE	hylococcus aureus F	ricella nidulans trpC	obacterium tuberculo Rv Rv 1610	dobacter sphaeroide 23 hisl	nebacterium glutam 19 hisF	nebacterium glutam 19 impA	nebacterium glutam 19 hisA	nebacterium glutam 19 hisH	ptomyces lividans 66
SEQ   Initial   Terminal   ORF   NO   (nt)   (nt)   (nt)   (bp)   (a a b)   (nt)   (nt)   (nt)   (bp)   (a a b)   (nt)   (nt)   (nt)   (bp)   (a a b)   (nt)   35	ļ	! 	Therr	Cam  4343	Arabi			Theri	Bacil	Stap	Eme	Myc. H37	Rho 1702	Cory	Con	Con	Con	Stre	
SEQ Initial Terminal (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt)	40		db Match	pir A72322	sp:HIPO_CAMJE	pir.S38197			prf.2513410A	SP. YFIE BACSU	sp.LGT_STAAU	sp.TRPG_EMENI	pir:H70556	sp:HIS3_RHOSH	sp.HIS6_CORG	prf.2419176B	gp:AF051846_1	gp:AF060558_1	
SEQ Initial TO (nt) (a.a.) SPEQ Initial TO (nt) (nt) (nt) SPEQ 2198475 25780 2198475 25781 2201584 25784 2201869 25784 2201869 25786 2205490 25786 2205490 25789 2209888 25790 2211875 5790 2212619 5794 2213273 5795 2215586			ORF (bp)	1284	1263	336	135	276	2550	900	948	801	657	354	774	825	738	633	1266
SEQ NO NO 5780 5781 5783 5783 5784 5786 5786 5786 5789 5799 5799 5799 5799 5799	45		Terminal (nt)	2199758	2201070	2201073	2201450	2201594	2201992	2204591	2207302	2208367	2209232	2209920	2210273	2211051		2212641	
0, = 0 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4, 4,	50		Initial (nt)	2198475	2199808	2201408	2201584	2201869		_1									
			SEQ	5780	5781	5782	5783	5784	5785	5786	5787	5788	5789	5790	5791	5792	· <del>· · · · · · · · · · · · · · · · · · ·</del>		
	55		SEQ	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295

10
15
20
25
30
35
40
45
50

۲	γ	<del></del>				-	_							_	- I			_		
	Function		imidazoleglycerol-phosph <b>at</b> e dehydratase	histidinol-phosphate aminotransferase	histidinol dehydrogenase	serine-rich secreted protein			histidine secretory acid phosphatase	tet repressor protein	glycogen debranching enzyme	hypothetical protein	oxidoreductase	myo-inositol 2-dehydrogenase	galactitol utilization operon repressor	ferrichrome transport ATP-binding protein or ferrichrome ABC transporter	hemin permease	iron-binding protein	iron binding protein	hypothetical protein
	Matched length (a a)		198	362	439	342			211	204	25%	258	268	343	329	246	332	103	182	113
	Similarity (%)		81.8	6.67	85.7	54.4			29.7	8.09	25.5	76.0	22.5	6'09	64.4	68.3	71.1	0.89	9.79	73.5
	Identity (%)		52.5	57.2	63.8	27.2			29.4	28.9	47.4	20.0	29.9	35.0	30.4	32.9	36.8	30.1	34.6	38.1
Table 1 (continued)	Homologous gene		Streptomyces coelicolor A3(2) hisB	Streptomyces coelicolor A3(2) hisC	Mycobacterium smegmatis ATCC 607 hisD	Schizosaccharomyces pombe SPBC215.13			Leishmania donovani SAcP-1	Escherichia coli plasmid RP1 tetR	Sulfolobus acidocaldarius treX	Mycobacterium tuberculosis H37Rv Rv2622	Streptomyces coelicolor A3(2) SC2G5.27c gip	Sinorhizobium meliloti idhA	Escherichia coli K12 galR	Bacillus subtilis 168 fhuC	Vibrio cholerae hutC	Bacillus subtilis 168 yvrC	Bacillus subtilis 168 yvrC	Escherichia coli K12 ytfH
	db Match	*	sp HIS7_STRCO	sp HIS8_STRCO	sp. HISX_MYCSM	gp:SPBC215_13			pri:2321269A	pir.RPECR1	BE852855 Hg	pir.E70572	gp:SC2G5_27	prf.2503399A	Sp. GALR_ECOLI	sp.FHUC_BACSU	pri:2423441E	pir:G70046	pir G70046	sp:YTFH_ECOLI
	ORF (bp)	225	909	1098	1326	1200	651	309	642	561	3588	801	774	1011	966	798	1038	348	594	441
	Terminal (nt)	2215639	2215869	2216494	2217600	2220358	2220459	2221919	2221187	2222518	2225835	2225949	2225990	2226769	2228901	2229099	2229900	2230947	2231339	2232016
	Initial (nt)	2215863	2216474	2217591	2218925	2219159	2221109	2221611	2221828	2221958	3222528	2225149	2226763	2227779	2227906	2229896	2230937	2231294	2231932	2232456
	SEO NO. (a a.)	5796	5797	5798	5799	5800	5801	5802	5803	5804	5885	5806	5807	5808	5809	5810	5811	5812	5813	5814
	SEQ NO. (DNA)	2296	2297	2298	2299	2300	2301	2302	2303	2304	3385	2306	2307	2308	2309	2310	2311	2312	2313	2314

	Function	DNA polymerase III epsilon chain		maltooligosyl trehalose synthase	hypothetical protein					alkanal monooxygenase alpha chain	hypothetical protein		maltooligosyltrehalose trehalohydrolase	hypothetical protein	threonine dehydratase			Corynebacterium glutamicum AS019	DNA polymerase III	chloramphenicol sensitive protein	histidine-binding protein precursor	hypothetical membrane protein
	Matched fength (a.a.)	355		814	322					375	120		268	214	436			415	1183	279	149	198
	Similarity (%)	50.1		68.6	528				! !	54.4	79.2		72 4	72.4	66.3			49.6	80.5	73.8	55.7	64.7
	Identity (%)	23.4		45.0	27.6					20.5	58.3		46.3	36.5	99.3			22.7	53.3	37.6	21.5	22.7
Table 1 (continued)	Homologous gene	Streptomyces coelicolor A3(2) SCIB. 12		Arthrobacter sp. Q36 treY	Deinococcus radiodurans DR1631					Photorhabdus luminescens ATCC 29999 luxA	Streptomyces coelicolor A3(2) SC7H2.05		Arthrobacter sp. Q36 treZ	Bacillus subtilis 168	Corynebacterium glutamicum ATCC 13032 ilvA			Catharanthus roseus metE	Streptomyces coelicolor A3(2) dnaE	Escherichia coli K12 rarD	Campylobacter jejuni D272 hisJ	Archaeoglobus fulgidus AF2388
	db Match	gp:SCI8_12	·	pir S65769	gp:AE002006_4		·			sp:LXA1_PHOLU	gp:SC7H2_5		pir:S65770	sp:YVYE_BACSU	sp:THD1_CORGL		,	pir:S57636	prf.2508371A	sp.RARD_ECOLI	sp:HISJ_CAMJE	pir:D69548
	ORF (bp)	1143	909	2433	1023	399	198	189	1056	1044	378	231	1785	651	1308	507	156	1203	3582	840	468	918
	Terminal (nt)	2234070	2234763	2237284	2238353	2238694	2239845	2240058	2239508	2241724	2241738	2242129	2244819	2242393	2244864	2246892	2246295	2247006	2248358	2252856	2253659	2254642
	Initial (nl)	2232928	2234158	2234852	2237331	2239092	5820 2240042	5821 2240246	2240563	2240681	2242115	2242359	2243035	2243043	2246171	2246386	2246450	2248208	2251939	2252017	2253192	2253725
•	SEO NO (a a)	5815	5816	5817	5818	5819	_	5821	5822	5823	5824	5825	5826	5827	5828	5829	5830	5831	5832	5833	5834	5835
	SEQ NO (DNA)	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335

						_							_								
5		U	enase or	Р)			nit se D	tidase		nce protein				le protein P	ne protein	10.			itase		· vo que canada de la canada de
10		Function	short chain dehydrogenase or general stress protein	diaminopimelate (DAP) decarboxylase	cysteine synthase		ribosomal large subunit pseudouridine synthase	lipoprotein signal peptidase		oleandomycin resistance protein		hypothetical protein	L-asparaginase	DNA-damage-inducible protein P	hypothetical membrane protein	transcriptional regulator		hypothetical protein	isoleucyl-tRNA synthetase		
15		Matched length (a.a.)	280	445	314		326	154		550		158	321	371	286	334		212	1066		
20		Similarity (%)	80.0	47.6	64.3		61.0	61.7		64.0		57.6	62.0	2 09	61.5	73.1		67.0	65.4		
		Identity (%)	48.2	22.9	32.8		36.5	33.8		36.4		36.7	31.2	31.8	315	44.3		42.0	38.5		
25	Table 1 (continued)	s gene	8 удаD	uginosa lysA	hus CH34		2 rluD	rescens NCIB		oioticus oleB		ropolis orf17	ŞI	2 dinP	2 ybiF	color A3(2)		color A3(2)	revisiae .S1		
30	Table 1 (c	Homologous gene	Bacillus subtilis 168 ydaD	Pseudomonas aeruginosa lysA	Alcaligenes eutrophus CH34 cysM	ĺ	Escherichia coli K12 rluD	Pseudomonas fluorescens NCIB 10586 IspA		Streptomyces antibioticus oleB		Rhodococcus erythropolis orf17	Bacillus licheniformis	Escherichia coli K12 dinP	Escherichia coli K12 ybiF	Streptomyces coelicolor A3(2) SCF51.06		Streptomyces caelicolor A3(2) SCF51.05	Saccharomyces cerevisiae A364A YBL076C ILS1		
<i>35</i>		db Match	sp.GS39_BACSU_E	sp:DCDA_PSEAE   F	sp.CYSM_ALCEU		sp:RLUD_ECOLI	Sp.LSPA_PSEFL F		pir.S67863		prf.2422382P	Sp. ASPG_BACLI E	sp:DINP_ECOLI E	sp:YBIF_ECOLI E	gp:SCF51_6		gp:SCF51_5	sp:SYIC_YEAST		
		ORF (bp)	876 sp	1287 sp.!	951 sp.(	579	930 sp:	534 sp.(	202	1650 pir	303	600 prf	5	1	858 sp:`	1002 gp.	132	627 gp.	3162 sp:	16	1095
45		Terminal O (It)	2254683 8	2255738 12	2258362 9	2259421 5	5360002	2260934 5	2262689 100	2264499 16	2265298 3	2264509 6	2266394 97	2266897 140	2268388 8	2269260 10	2270435 1	2270258 6	2270988 31	2274473 21	2274767 10
50		Initial (nt)	2255558	2257024	2259312	2259999	2260931	2261467	2261688	2262850	2264996	2265108	2265420	2268297	2269245	2270261	2270304	2270884	2274149	2274688	2275861
		SEQ NO (a.a.)	5836	5837	5838	5839	5840	5841	5842	5843	5844	5845	5846	5847	5848	5849	5850	5851	5852	5853	5854
55		SEQ NO.	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354

						Table 1 (continued)				
SEQ NO (DNA)	SEQ NO (a a)	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched length (a.a.)	Function
2355	5855	2276637	2276353	285	pir:F70578	Mycobacterium tuberculosis H37Rv Rv2146c	46.3	73.2	82	hypothelical membrane protein
2356	5856	2277336	2276881	456	gp:BLFTSZ_6	Brevibacterium lactofermentum orf6	99.3	99.3	152	hypothetical protein (putative YAK 1 protein)
2357	5857	2278078	2277416	663	sp YFZ1_CORGL	Corynebacterium glutamicum	97.7	9.66	221	hypothetical protein
2358	5858	2278859	2278122	738	pri.2420425C	Brevibacterium lactofermentum yfih	99.2	100.0	246	hypothetical protein
2359	5859	2279155	2279640	486	GP_AB028868_1	Mus musculus P4(21)n	39.0	51.0	117	hypothetical protein
2360	5860	2280215	2278890	1326	sp.FTSZ_BRELA	Brevibacterium lactofermentum fts2	98.6	98.6	442	cell division protein
2361	5861	2281135	2280470	999	gsp:W70502	Corynebacterium glutamicum ftsQ	98.6	100.0	222	cell division initiation protein or cell division protein
2362	5862	2282623	2281166	1458	gp:AB015023_1	Corynebacterium glutamicum murC	99.4	8.66	486	UDP-N-acetylmuramatealanine ligase
2363	5863	2283776	2282661	1116	gp:BLA242646_3	Brevibacterium lactofermentum ATCC 13869 murG	98.9	99.5	372	UDP-N-acetylglucosamine-N-acetylmuramyt-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine pyrophosphoryl-undecaprenol N-acetylglucosamine
2364	5864	2285431	2283782	1650	gp.BLA242646_2	Brevibacterium lactofermentum ATCC 13869 ftsW	99.4	9.66	490	cell division protein
2365	5865	2285904	2285437	468	gp:BLA242646_1	Brevibacterium lactofermentum ATCC 13869 murD	99.1	99.1	110	UDP-N-acetylmuramoylalanine-D- glutamate ligase
2366	5866	2286272	2286655	384						
2367	5867	2286499	2286831	333						
2368	5868	2287959	2286862	1098	sp:MRAY_ECOLI	Escherichia coli K12 mraY	38.6	63.8	365	phospho-n-acetylmuramoyl- pentapeptide
2369	5869	2289510	2287969	1542	sp MURF_ECOLI	Escherichia coli K12 murF	35.0	64.2	494	UDP-N-acetylmuramoylalanyl-D- glutamyl-2,6-diaminopimelate-D- alanyl-D-alanyl ligase

5		Function	UDP-N-acetylmuramoylalanyl-D- glutamyl-2,6-diaminopimelate-D- alanyl-D-alanyl ligase	penicillin binding protein	penicillin-bınding protein		hypothetical protein	hypothetical membrane protein	hypothetical protein		hypothetical protein	5,10-methylenetetrahydrofolate reductase	dimethylallyltranstransferase	hypothetical membrane protein		hypothetical protein	eukaryotic-type protain kinase		hypothetical membrane protein
15		Matched length (a.a.)	491	57	650		323	143	137		190	303	329	484		125	684	`	411
20		Similarity (%)	9'.29	100.0	58.8		79.3	88.8	69.3		65.3	9.02	62.0	9.69		68.8	62.4		58.4
		Identity (%)	37.7	100.0	28.2		55.1	72.0	39.4		36.3	42.6	30.1	35.7		43.2	34.2		30.7
25	lable I (continued)	Homologous gene	Bacillus subtilis 168 murE	Brevibacterium lactofermentum ORF2 pbp	Pseudomonas aeruginosa pbpB		Mycobacterium tuberculosis H37Rv Rv2165c	Mycobacterium leprae MLCB268.11c	Mycobacterium tuberculosis H37Rv Rv2169c		Mycobacterium leprae MLCB268.13	Streptomyces lividans 1326 metF	Myxococcus xanthus DK 1050 ORF1	Mycobacterium leprae MLCB268.17		Mycobacterium tuberculosis H37Rv Rv2175c	Streptomyces coelicolor A3(2) pkaF		Mycobacterium leprae MLCB268.23
. F		Ÿ	Bacillus su	Brevibacte ORF2 pbp	Pseudomo		Mycobacterium t H37Rv Rv2165c	Mycobacte MLCB268	Mycobacterium t H37Rv Rv2169c		Mycobact MLCB268	Streptomy metF	Myxococc ORF1	Mycobacteriu MLCB268.17		Mycobacterium to H37Rv Rv2175c	Streptomy pkaF		Mycobact MLCB268
40		db Match	sp:MURE_BACSU	GSP:Y33117	pir:S54872		pir.A70581	gp:MLCB268_11	pir:C70935		gp:MLCB268_13	sp:METF_STRLI	pir:S32168	gp:MLCB268_16		pir.A70936	gp:AB019394_1		gp:MLCB268_21
		ORF (bp)	1551	225	1953	795	1011	429	387	423	573	978	1113	1470	507	369	2148	651	1236
45		Terminal (nt)	2289523	2290973	2291212	2293323	2294117	2295376	2296512	2297231	2298438	2298451	2300636	2302175	2302685	2302251	2304980	2303040	2306218
50		Initial (nt)	2291073	2291197	2293164	2294117	2295127	2295804	2296898	2297653		2299428	2299524	2300706	2302179	2302619	2302833	2303690	5886 2304983
		SEQ NO.	5870	1285	5872	5873	5874	5875	5876	5877	5878	5879	5880	5881	5882	5883	5884	5885	
55		SEQ.	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

	Function	hypothetical membrane protein	3-deoxy-D-arabino-heptulosonate-7 phosphate synthase	hypothetical protein	hypothetical membrane protein	major secreted protein PS1 protein precursor			hypothetical membrane protein	acyltransferase	glycosyl transferase	protein P60 precursor (invasion- associated-protein)	protein P60 precursor (invasion-associated-protein)	ubiquinol-cytochrome c reductase cytochrome b subunit	ubiquinol-cytochrome c reductase iron-sultur subunit (Rieske [eFe-2S] iron-sultur protein cyoB	ubiquinol-cytochrome c reductase cytochrome c
	Matched length (a.a.)	434	462	166	428	440			249	245	383	296	191	201	203	278
	Similarity (%)	62.0	6 /8	777	64.5	57.1			100.0	100.0	7.5.7	8.09	61.3	64.7	57.1	83.1
	Identity (%)	30.4	6.99	58.4	35.1	28.2			100.0	100.0	50.1	26.4	33.0	34.3	37.9	58.6
Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv2181	Amycolatopsis mediterranei	Mycobacterium leprae MLCB268.21c	Mycobacterium tuberculosis H37Rv Rv2181	Corynebacterium glutamicum (Brevibacterium flavum) ATCC 17965 csp1			Corynebacterium glutamicum ATCC 13032	Corynebacterium glutamicum ATCC 13032	Streptomyces coelicolor A3(2) SC6G10.05c	Listeria ivanovii iap	Listeria grayi iap	Heliobacillus mobilis petB	Streptomyces lividans qcrA	Mycobacterium tuberculosis H37Rv Rv2194 qcrC
	db Match	pir.G70936	gp.AF260581_2	gp.MLCB268_20	pir:G70936	sp.CSP1_CORGL			gp.AF096280_3	gp.AF096280_2	gp:SC6G10_5	sp:P60_LISIV	sp:P60_LISGR	prf.2503462K	gp:AF107888_1	sp:Y005_MYCTU
	ORF (bp)	1308	1386	504	2418	1449	204	177	1188	735	1143	1047	627	1602	672	885
	Terminal (nt)	2307621	2307697	2309173	2312252	2313808	2314036	2313916	2314236	2315678	2317633	2318804	2319968	2321472	2323088	2324311
	Initial (nt)	2306314	2309082	2309676	2309835	2312360	2313833	2314092	2315423	2316412	2318775	2319850	2320594	2323073	2323759	2325195
	SEQ NO.	5887	5888	5889	5890	5891	5892	5893	5894	5895	5896	5897	5898	5899	5900	5901
	SEQ NO. (DNA)	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398	2399	2400	2401

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

100	<b>⊢</b>					Table 1 (continued)				
SEQ NO.	NO (a a.)	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched length (a.a.)	Function
2402	5902	2325887	2325273	615	Sp.COX3_SYNVU	Synechococcus vulcanus	36.7	70.7	188	cytochrome c oxidase subunit III
2403	5903	2326273	2326121	153						
2404	5904	2326900	2326472	429	sp:Y00A_MYCTU	Mycobacterium tubercutosis H37Rv Rv2199c	38.6	71.0	145	hypothetical membrane protein
2405	5905	2327997	2326921	1077	sp.COX2_RHOSH	Rhodobacter sphaeroides ctaC	28.7	53.9	317	cytochrome c oxidase subunit II
2406	9069	2328516	2330435	1920	1920 gp. AB029550_1	Corynebacterium glutamicum KY9611 ItsA	99.7	93.8	640	glutamine-dependent amidotransferase or asparagine synthetase (lysozyme insensitivity protein)
2407	5907	2330927	2330586	342	gp:AB029550_2	Corynebacterium glutamicum KY9611 orf1	100.0	100.0	114	hypothetical protein
2408	5908	2331200	2331967	768	gp:MLCB22_2	Mycobacterium leprae MLCB22.07	35.0	60.2	246	hypothetical membrane protein
2409	5909	2331974	2332495	522	pir.S52220	Rhodobacter capsulatus cobP	43.0	64.0	172	cobinamide kinase
2410		5910 2332512	2333600	1089	sp.COBU_PSEDE	Pseudomonas denitrificans cobU	37.8	6.99	341	nicotinate-nucleotide dimethylbenzimidazole phosphoribosyltransferase
2411	5911	2333615	2334535	921	sp.COBV_PSEDE	Pseudomonas denitrificans cobV	25.3	49.8	305	cobalamin (5'-phosphate) synthase
2412		5912 2334717	2334481	237						
2413	5913	2335741	2335028	714	prf.2414335A	Streptomyces clavuligerus car	38.6	68.5	241	clavulanate-9-aldehyde reductase
2414	5914	2337051	2335915	1137	sp:ILVE_MYCTU	Mus musculus BCAT1	40.1	70.3	364	branched-chain amino acid aminotransferase
2415	5915	2337235	2338734	1500	gp.PPU010261_1	Pseudomonas putida ATCC 12633 pepA	36.3	629	493	leucyl aminopeptidase
2416	5916	2339140	2338748	393	prf.2110282A	Saccharopolyspora erythraea ORF1	40.2	0.79	97	hypothetical protein
2417	5917	2339269	2341293	2025	gp:AF047034_2	Streptomyces seoulensis pdhB	48.9	68.5	691	dihydrolipoamide acetyltransferase
2418	5918	2340804	2339440	1365		ſ				
2419	5919	2341412	2342164	753	gp.AB020975_1	Arabidopsis thaliana	36.7	65.7	210	lipoyltransferase

5		Function	lipoic acid synthetase	hypothetical membrane protein	hypothetical membrane protein	transposase (ISCg2)		hypothetical membrane protein		mutator mutT domain protein	hypothetical protein		alkanal monooxygenase alpha chair (bacterial luciferase alpha chain)	protein synthesis inhibitor (translation initiation inhibitor)			4-hydroxyphenylacetate permease	fransmembrane transport protein	transmembrane transport protein		
15		Matched length (a.a.)	285	257	559	401		157		145	128		220	111			433	158	118		
20		Similarity (%)	70.9	76.7	8.79	100.0		63.7		44.0	65.6		6.09	73.0			53.4	72.8	66.1		
		Identity (%)	44.6	45.5	32.9	100.0		41.4		31.0	36.7		25.0	40.5			21.9	42.4	31.4	•	
30	Table 1 (continued)	Homologous gene	Pelobacter carbinolicus GRA BD 1 lipA	Mycobacterium tuberculosis H37Rv Rv2219	Escherichia coli K12 yidE	Corynebacterium glutamicum ATCC 13032 tnp		Streptomyces coelicolor A3(2) SC5F7.04c		•	Thermotoga maritima MSB8 TM1010		Vibrio harveyi luxA	Thermotoga maritima MSB8 TM0215			Escherichia coli hpaX	Streptomyces coelicolor A3(2) SCGD3.10c	Streptomyces coelicolor A3(2) SCGD3 10c		
35	-	Ĭ	Pelobact 1 lipA	Mycobacterium H37Rv Rv2219	Escheric	Corynebacterium ATCC 13032 tnp		Streptom SC5F7.0			Thermoto TM1010		Vibrio ha	Thermoto TM0215			Escherich	Streptomyce SCGD3.10c	Streptomyce SCGD3 10c		
40		db Match	sp.LIPA_PELCA	sp:Y00U_MYCTU	sp.YIDE_ECOLI	gp:AF189147_1		gp:SC5F7_34			pir.872308		Sp:LUXA_VIBHA	pir.A72404			prf.2203345H	gp:SCGD3_10	gp:SCGD3_10		
		ORF (bp)	1044	780	1617	1203	300	471	213	975	399	900	849	393	243	261	1323	561	444	195	405
45		Terminal (nt)	2343347	2344258	2346047	2346289	2347804	234,8078	2350408	2351996	2350912	2351310	2352828	2353225	2355398	2355180	2356843	2357354	2357707	2357290	2358130
50 ·		initial (nt)	2342304	2343479	2344431	2347491	2347505	2348548	2350620	2351022	2351310	2351909	2351980	2352833	2355156	2355440	2355521	2356794	2357264	2357484	2357726
		SEQ NO (a a.)	5920	5921	5922	5923	5924	5925	5926	5927	5928	5929	5930	5931	5932	5933	5934	5935	5936	5937	5938
55		SEQ NO.	2420	2421	2422	2423	2424	2425	2426	2427	2428	2429	2430	2431	2432	2433	2434	2435	2436	2437	2438

low molecular weight protein-tyrosine-phosphatase

156

63.5

46.2

Streptomyces coelicolor A3(2) SCQ11.04c ptpA

sp.PTPA\_STRCO

471

2375684

2375214

5952 5953 5954

2452

2450 2451 insertion element (1S402)

129

hypothetical protein

281

65.5 9.99

40.9 32.6

Mycobacterium tuberculosis H37Rv Rv2235

sp:Y01G\_MYCTU sp:YI21\_BURCE

954

2376720

5955 2375767

Burkholderia cepacia

393

5956 2377390 2376998

2456

5
10
15
20
25
30
35
40
45
50

SEQ NO.

2441

2443

2446 2447 2448

_																
	Function		heme oxygenase	glutamate-ammonia-ligase adenylyltransferase	glutamine synthetase	hypothetical protein	hypothetical protein	hypothetical protein	galactokinase	virulence-associated protein		bifunctional protein (ribonuclease H and phosphoglycerate mutase)		hypothetical protein	hypothetical protein	phosphoglycolate phosphatase
	Matched length (a a )		214	808	441	392	601	54	374	358		382		249	378	204
	Similarity (%)		78.0	0.79	73.0	54.1	58.2	55.6	53.7	54.5		75.1		58.6	76.2	54.4
	Identity (%)		67.9	43.4	43.5	26.8	33.4	38.9	24.9	27.1		54.7		26.5	49.2	26.0
Table 1 (continued)	Homologous gene		Corynebacterium diphtheriae C7 hmuO	Streptomyces caelicolor A3(2) glnE	Thermotoga maritima MSB8 glnA	Streptomyces coelicolor A3(2) SCE9.39c	Mycobacterium tuberculosis H37Rv Rv2226	Streptomyces coelicolor A3(2) SCC75A.11c.	Homo sapiens galK1	Brucella abortus vacB		Mycobacterium fuberculosis H37Rv Rv2228c		Mycobacterium tuberculosis H37Rv Rv2229c	Mycobacterium tuberculosis H37Rv Rv2230c	Escherichia coli K12 gph
	db Match		sp:HMUO_CORDI	15 gp:SCY17736_4	Sp.GLNA_THEMA	gp:SCE9_39	sp:Y017_MYCTU	gp:SCC75A_11	sp:GAL1_HUMAN	gp:AF174645_1		16 sp.Y019_MYCTU		sp:Y01A_MYCTU	sp.Y018_MYCTU	sp:GPH_ECOLI
	ORF (bp)	543	645	3135	1338	1104	1827	180	1293	1266	486	1146	729	717	1140	654
	Terminal (nt)	2358153	2358772	2359614	2362818	2365455	2367413	2367473	2369083	2369116	2370908	2371412	2373289	2372573	2373323	2375197
	Initial (nt)	2358695	2359416	2362748	2364155	2364352	2365587	2367652	2367791	2370381	2370423	2372557	2372561	2373289	2374462	2374544
	SEQ NO.	5939	5940	5941	5942	5943	5944	5945	5946	5947	5948	5949	2950	5951	5952	5953
	7 3	G)	0	I _	1 ~	. m	4	10	10	1	8	6	0	<b>—</b>	~	6

5		
10		
15		
20		
25		
30	-	
35		
40		
45		
50		

ed)	
continued)	
<u>0</u>	
Table 1	
Ta	

	Function		transcriptional regulator		hypothetical protein		pyruvate dehydrogenase component		ABC transporter or glutamine transport ATP-binding protein		ribose transport system permease protein	hypothetical protein	calcium binding protein		lipase or hydrolase	acyl carier protein	N-acetylglucosamine-6-phosphate deacetylase	hypothetical protein	
	Matched length (a a)		135 tran		134 hyp		910 pyru		261 ABC		283 ribose to protein	286 hyp	125 calc		352 lipa	75 acy	253 N-a	289 hур	
-	Similarity M (%)		57.8		77.6	-	78.9		62.8		58.7	62.9	55 2		55.7	80.0	75.5	65.7	
-	Identity (%)		30.4		55.2		55.9		33.7		25.4	26.2	41.6		29.6	42.7	43.9	33.6	
(	Homologous gene		Streptomyces coelicolor A3(2) SC8F4.22c		Mycobacterium tuberculosis H37Rv Rv2239c		Streptomyces seoulensis pdhA		Escherichia coli K12 glnQ		Bacillus subtilis 168 rbsC	Rickettsia prowazekii Madrid E RP367	Dictyostelium discoideum AX2 cbpA		Streptomyces coelicolor A3(2) SC6G4.24	Myxococcus xanthus ATCC 25232 acpP	Escherichia coli K12 nagD	Deinococcus radiodurans DR1192	
	db Match		gp:SC8F4_22		Sp:Y01K_MYCTU		gp. AF047034_4		sp.GLNQ_ECOLI		sp:RBSC_BACSU	pir:H71693	sp.CBPA_DICDI		gp:SC6G4_24	sp:ACP_MYXXA	sp:NAGD_ECOL!	gp:AE001968_4	
	ORF (bp)	243	378	198	429	345	2712	1476	789	963	888	939	810	372	1014	291	825	1032	471
	Terminal (nt)	2377484	2378276	2378489	2378884	2379770	2382744	2380765	2382827	2385426	2383622	2384509	2386580	2385913	2386614	2387957	2388821	2389869	2390434
	Initial (nt)	2377726	2377899	2378292		2379426	5962 2380033	2382240		2384464	2384509	2385447	2385771	2386284	2387627	2387667	2387997	2388838	2390904
	SEQ	5957	5958	5959	5960	5961	5962	5963	5964	5965	9969	5967	5968	5969	5970	5971	5972	5973	5974
	SEQ	2457	2458	2459	2460	2461	2462	2463	2464	2465	2466	2467	2468	2469	2470	2471	2472	2473	2474

	Function	hypothetical protein						alkaline phosphatase D precursor		hypothétical protein	hypothetical protein		DNA primase	ribonuclease Sa			L-glutamine D-fructose-6-phosphate amidotransferase			deoxyguanosinetriphosphale triphosphohydrolase	hypothetical protein
	Matched length (a a)	271						530		594	89		633	86			989	1		414	171
	Similarity (%)	75.3						64.7		73.1	72.1		82.9	67.4			82.2			76.3	59 7
	Identity (%)	52.4						34.2		44.4	41.2		59.1	49.0			59.1			54.6	30.4
Table 1 (continued)	Homologous gene	Streptomyces coelicolor A3(2) SC4A7.08						Bacillus subtilis 168 phoD		Streptomyces coelicolor A3(2) SCI51.17	Mycobacterium tuberculosis H37Rv Rv2342		Mycobacterium smegmatis dnaG	Streptomyces aureofaciens BMK			Mycobacterium smegmatis mc2155 glmS			Mycobacterium smegmatis dgt	Neisseria meningitidis NMA0251
	db Match	gp:SC4A7_8						sp PPBD_BACSU		gp:SCI51_17	pir:G70661		prf.2413330B	gp:XXU39467_1			gp:AF058788_1			prf.2413330A	gp:NMA122491_23
	ORF (bp)	825	492	771	546	465	342	1560	714	1836	240	675	1899	462	243	636	1869	324	1152	1272	675
	Terminal (nt)	2391184	2392075	2392579	2393970	2393973	2394935	2396763	2395273	2399099	2399397	2399668	2399405	2401834	2402080	2402530	2402144	2404846	2406822	2404987	2406262
	Initial (nt)	2392008	2392566	2393349	2393425	2394437	2394594	2395204	2395986	2397264	2399158	2400342	2401303	2401373	2401838	2403165	2404012	2404523	2405671	2406258	2494 5994 2406936
	SEQ NO. (a.a.)	5975	5976	5977	5978	5979	5980	5981	5982	5983	5984	5985	5986	2987	5988	5989	5990	5991	5992	5993	5994
	SEQ NO. (DNA)	2475	2476	2477	2478	2479	2480	2481	2482	2483	2484	2485	2486	2487	2488	2489	2490	2491	2492	2493	2494

.

5
10
15
20
25
30
35
40
45
50

_
$\mathbf{\tau}$
밇
п.
=
$\rightarrow$
=
_
-=
_
₻
_
00
•
۲١
_
$\overline{}$
_
Ψ-
4
9
-
五
_
Ē
,-•
$\overline{}$

ī			-	7				$\neg \neg$		ارو								
	Function	hypothetical protein	hypothetical protein		glycyl-tRNA synthetase	bacterial regulatory protein, arsR family	ferric uptake regulation protein	hypothetical protein (conserved in C. glutamicum?)	hypothetical membrane protein	undecaprenyl diphosphate synthase	hypothetical protein	Era-like GTP-binding protein	hypothetical membrane protein	hypothetical protein	Neisserial polypeptides predicted to be useful antigens for vaccines and dragnostics	phosphate starvation inducible protein	hypothetical protein	
	Matched length (a a)	692	138		508	89	132	529	224	233	245	296	432	157	85	344	248	
	Similarity (%)	63.6	54.4		6.69	73.0	70.5	46.7	0.79	71.2	74.3	70.3	82.4	86.0	20.0	84.6	75.4	
	identity (%)	31.1	24.6		46.1	49.4	34.9	24.8	40.6	43.4	45.7	39.5	52.8	65.0	45.0	61.1	44.0	
Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv2345	Drosophila melanogaster CG10592		Thermus aquaticus HB8	Mycobacterium tuberculosis H37Rv Rv2358 furB	Escherichia coli K12 fur	Mycobacterium tuberculosis H37Rv Rv1128c	Streptomyces coelicolor A3(2) h3u	Micrococcus luteus 8-P 26 uppS	Mycobacterium tuberculosis H37Rv Rv2362c	Streptococcus pneumoniae era	Mycobacterium tuberculosis H37Rv Rv2366	Mycobacterium tuberculosis H37Rv Rv2367c	Neisseria meningitidis	Mycobacterium tuberculosis H37Rv Rv2368c phoH	Streptomyces coelicolor A3(2) SCC77.19c.	-
	db Match	pir B70662	gp:AE003565_26		pir.S58522	pir:E70585	sp.FUR_ECOLI	pir.A70539	gp:AF162938_1	sp:UPPS_MICLU	pir.A70586	gp:AF072811_1	sp.Y1DE_MYCTU	sp:YN67_MYCTU	GSP:Y75650	sp:PHOL_MYCTU	gp:SCC77_19	
	ORF (bp)	2037	486	582	1383	369	432	1551	792	729	726	915	1320	588	264	1050	723	942
	Terminal (nt)	2409029	2409779	2410280	2410956	2412948	2413423	2415118	2415298	2416371	2417222	2417969	2418990	2420313	2421236	2420900	2421975	2423791
	Initial (nt)	2406993	2410264	2410861	2412338	2412580	2412992	2413568	2416089	2417099	2417947	2418883	2420309	2420900	2420973	2421949	2422697	2422850
	SEQ NO (a.a.)	5995	9669	5997	5998	5999	0009	6001	6002	6003	6004	6005	9009	6007	6008	6009	6010	1109
	SEQ NO (DNA)	2495	2496	2497	2498	2499	2500	2501	2502	2503	2504	2505	2506	2507	2508	2509	2510	2511

3
10
15
20
25
<i>30</i>
35
40
45
50

	Function	heat shock protein dnaJ	heat-inducible transcriptional repressor (groEL repressor)	oxygen-independent coproporphyrinogen III oxidase	agglutinin attachment subunit precursor			long-chain-fatty-acidCoA ligase	4-alpha-glucanotransferase	ABC transporter, Hop-Resistance protein	Neisserial polypeplides predicted to be useful antigens for vaccines and diagnostics	polypeptides predicted to be useful antigens for vaccines and diagnostics			peptidyl-dipeptidase	carboxylesterase	glycosyl hydrolase or trehalose synthase	hypotnetical protein
	Matched length (a.a.)	380	334	320	134			611	738	604	68	107			069	453	594	449
	Similarity (%)	77.4	79.6	64.1	64.9			75.1	55.4	64.4	51.0	53.0			68.3	45.7	84.9	58 8
	Identity (%)	47.1	48.2	33 1	36.6			48.0	28.3	29.5	44.0	47.0			40.3	24.1	65.2	32.1
Table 1 (continued)	Homologous gene	Streptomyces albus dnaJ2	Streptomyces albus hrcA	Bacillus stearothermophilus hemN	Saccharomyces cerevisiae YNR044W AGA1			Streptomyces coelicolor A3(2) SC6G10.04	Escherichia coli K12 malQ	Lactobacillus brevis plasmid horA	Neisseria gonorrhoeae	Neisseria meningitidis			Salmonella typhimurium dcp	Anisopteromalus calandrae	Mycobacterium tuberculosis H37Rv Rv0126	Mycobacterium tuberculosis H37Rv Rv0127
	db Match	prf.2421342B	1023 prf.2421342A	prf:2318256A	sp.AGA1_YEAST			gp:SC6G10_4	sp:MALQ_ECOLI	1863 gp. AB005752_1	GSP:Y74827	GSP:Y74829			sp:DCP_SALTY	gp. AF064523_1	pir:G70983	pir:H70983
	ORF (bp)	1146	1023	066	519	693	378	1845	2118	1863	255	333	180	204	2034	1179	1794	1089
	Terminal (nt)	2422700	2423915	2424965	2426699	2426776	2427807	2428184	2432413	2434370	2433614	2433875	2434440	2434573	2434805	2438049	2439906	2440994
	initial (nt)	2423845	2424937	2425954	2426181	2427468	2428184	2430028	2430296	2432508	2433868	2434207	6023 2434619	2434776	2436838	2436871	6027 2438113	6028 2439906
	SEQ NO (a a.)	6012	6013	6014	6015	6016	6017	6018	6019	6020	6021	6022		6024	6025	6026	6027	6028
	SEQ NO.	2512	2513	2514	2515	2516	2517	2518	2519	2520	2521	2522	2523	2524	2525	2526	2527	2528

5	٠
10	
15	
20	
25	
30	
35	
40	
45	
50	

		<del></del>	T .			-					<del>,                                     </del>	,			·						
	Function	isopentenyl-diphosphate Delta- isomerase						beta C-S lyase (degradation of aminoethylcysteine)	branched-chain amino acid transport system carrier protein (isoleucine uptake)	alkanal monooxygenase alpha chain		malonate transporter	glycolate oxidase subunit	transcriptional regulator		hypothetical protein		heme-binding protein A precursor (hemin-binding lipoprotein)	oligopeptide ABC transporter (permease)	dipeptide transport system permease protein	oligopeptide transport ATP-binding protein
	Matched length (a a)	189						325	426	343		324	483	203		467		546	315	271	372
	Similarity (%)	57.7						100.0	100.0	49.0		60.5	55.1	65.0		57.6		55.5	73.3	74 5	66.4
	Identity (%)	31.8						99.4	8:66	216		25.9	27.7	25.6		22.5		27.5	40.0	43.2	37.4
Table 1 (continued)	Homologous gene	Chlamydomonas reinhardtii ipi1						Corynebacterium glutamicum ATCC 13032 aecD	Corynebacterium glutamicum ATCC 13032 brnQ	Vibrio harveyi luxA		Sinorhizobium meliloti mdcF	Escherichia coli K12 glcD	Escherichia coli K12 ydfH		Salmonella typhimurium ygiK		Haemophilus influenzae Rd HI0853 hbpA	Bacillus subtilis 168 appB	Escherichia coli K12 dppC	Escherichia coli K12 oppD
	db Match	pir.T07979						gp:CORCSLYS_1	sp.BRNQ_CORGL	Sp.LUXA_VIBHA		gp:AF155772_2	sp GLCD_ECOLI	sp:YDFH_ECOLI		sp:YGIK_SALTY		sp:HBPA_HAEIN	sp.APPB_BACSU	sp:DPPC_ECOLI	prf 2306258MR
	ORF (bp)	585	222	438	1755	999	519	975	1278	978	522	927	2844	711	282	1347	423	1509	996	828	1437
	Terminal (nt)	2441005	2441890	2442792	2441602	2443356	2444033	2445709	2446993	2447998	2450323	2450859	2451794	2455435	2455452	2455720	2457337	2459371	2460336	2461167	2462599
	Initial (nt)	2441589	2441669	2442355	2443356	2444015	2444551	2444735	2445716	2447021	2450844	2451785	2454637	2454725	2455733	2457066	2457759	2457863	2459371	2460340	2461163
	SEQ NO.	6058	6030	6031	6032	6033	6034	6035	6036	6037	6038	6039	6040	6041	6042	6043	6044	6045	6046	6047	6048
	SEQ NO. (DNA)	2529	2530	2531	2532	2533	2534	2535	2536	2537	2538	2539	2540	2541	2542	2543	2544	2545	2546	2547	2548

10
15
20
25
30
35
40
45

_												<del></del> -		-						
	Function	hypothetical protein	hypothetical protein	ribose kinase	hypothetical membrane protein		sodium-dependent transporter or odium Bile acid symporter family	apospory-associated protein C		thiamine biosynthesis protein x	hypothetical protein	glycine betaine fransporter				large integral C4-dicarboxylate membrane transport protein	small integral C4-dicarboxylate membrane transport protein	C4-dicarboxylate-binding periplasmic protein precursor	extensin l	GTP-binding protein
	Matched length (a.a.)	106	157	300	466		284	295		133	197	601				448	118	227	46	603
	Similarity (%)	44.0	58.0	65.0	64.6		61.6	51.2		100 0	65.5	71.7				71.9	73.7	99 0	73.0	83.6
	identity (%)	35.0	29.3	41.0	39.9		31.3	28.5		100.0	42.6	39.8				34.6	33.9	28.2	63.0	58.7
Table 1 (continued)	Homologous gene	Aeropyrum pernix K1 APE1580	Aquifex aeolicus VF5 aq_768	Rhizobium etli rbsK	Streptomyces coelicolor A3(2) SCM2.16c		Homo sapiens	Chlamydomonas reinhardtii		Corynebacterium glutamicum ATCC 13032 thiX	Mycobacteriophage D29 66	Corynebacterium glutamicum ATCC 13032 betP				Rhodobacter capsulatus dctM	Klebsiella pneumoniae dctQ	Rhodobacter capsulatus B10 dctP	Lycopersicon esculentum (tomato)	Bacillus subtilis 168 lepA
	db Match	PIR:G72536	pir.D70367	prf:2514301A	gp:SCM2_16		sp:NTCI_HUMAN	gp:AF195243_1		sp.THIX_CORGL	sp:VG66_BPMD	sp.BETP_CORGL				prf.2320266C	gp:AF186091_1	sp.DCTP_RHOCA	PRF:1806416A	sp:LEPA_BACSU
	ORF (bp)	507	549	903	1425	303	972	846	366	929	588	1890	966	1608	384	1311	480	747	243	1845
ļ	Terminal (nt)	2461543	2462602	2464143	2465768	2465465	2466038	2467922	2470678	2472819	2472893	2475542	2477492	2479251	2479762	2479898	2481213	2481734	2484087	2482548
	Initial (nt)	2462049	2463150	2463241	2464344	2465767	2467009	2467077	2470313	2472250	2473480	2473653	2476497	2477644	2479379	2481208	2481692	2482480	2483845	2484392
	SEQ NO (a a)	6049	6050	6051	6052	6053	6054	6055	9509	2509	6058	6909	909	6061	6062	6063	6064	9099	9909	6067
	SEQ NO (DNA)	2549	2550	2551	2552	2553	2554	2555	2556	2557	2558	2559	2560	2561	2562	2563	2564	2565	2566	2567

5	Function	hypothetical protein	30S ribosomal protein S20	thrreonine efflux protein	ankyrin-like protein	hypothetical protein	late competence operon required for DNA binding and uptake	late competence operon required for DNA binding and uptake		hypothetical protein hypothetical protein	phosphoglycerate mutase	hypothetical protein	hypothetical protein		gamma-glutamyl phosphate reductase or glutamate-5- semialdehyde dehydrogenase	D-isomer specific 2-hydroxyacid dehydrogenase		GTP-binding protein
	Matched length (a.a.)	185 hy	85 31	210 th	129 ar	313 h	527 la	195 la	,	273 h	235 pl	117 h	197 h		432 re	304 d D		487 G
20	Similarity (%)	69.7	72.9	67.1	80.6	74.1	49.7	63.6		. 6.99	66.4	86.3	853		8.66	100.0		78.2
	Identity (%)	41.6	48.2	30.0	61.2	46.0	21.4	30.8		34.8	46.8	55 6	0.89		99.1	99.3		58.9
Table 1 (continued)	s gene	oerculosis	12 rps T	12 rhtC	licolor A3(2)	oerculosis	8 comEC	в сомЕА		licolor A3(2)	berculosis	berculosis	licolor A3(2)		glutamicum	glutamicum Ih		licolar A3(2)
Table 1 ((	Homologous gene	Mycobacterium tuberculosis H37Rv Rv2405	Escherichia coli K12 rpsT	Escherichia coli K12 rhtC	Streptomyces coelicolor A3(2) SC6D7.25.	Mycobacterium tuberculosis H37Rv Rv2413c	Bacillus subtilis 168 comEC	Bacillus subtilis 168 comEA		Streptomyces coelicolor A3(2)	Mycobacterium tuberculosis H37Rv Rv2419c	Mycobacterium tuberculosis H37Rv Rv2420c	Streptomyces coelicolor A3(2) SCC123.17c		Corynebacterium glutamicum ATCC 17965 proA	Corynebacterium glutamicum ATCC 17965 unkdh		Streptomyces coelicolor A3(2) obg
35		ΣÏ			ភ ភ	ΣI				∞ • ∞	ΣÏ	ΣÏ						छ <del>।</del>
40	db Malch	pir:H70683	sp:RS20_ECOLI	sp.RHTC_ECOL	gp:SC6D7_25	pir:H70684	sp:CME3_BACSU	sp:CME1_BACSU		gp: \$66123_7	pir.F70685	pir:G70685	gp:SCC123_17		sp.PROA_CORGL	sp. YPRA_CORGL		gp.D87915_1
	ORF (bp)	609	261	699	405	975	1539	582	822	823	708	471	678	1023	1296	912	711	1503
45	Terminal (nt)	2485269	2485733	2485801	2486477	2486910	2487912	2489573	2491732	2498298	2491151	2491873	2492501	2493215	2494339	2495696	2497513	2498009
50	Initial (nt)	2484661	2485473	2486469	2486881	2487884	2489450	2490154	2490911	2481111	2491858	2492343	2493178	2494237	2495634	2496607	2496803	2499511
	SEQ NO (a.a.)	6068	6909	0209	6071	6072	6073	6074	6075	8878	6077	6078	6209	6080	6081	6082	6083	6084
55	SEQ NO (DNA)	2568	2569	2570	2571	2572	2573	2574	2575	3578	2577	2578	2579	2580	2581	2582	2583	2584

5	
10	
15	
20	
25	
30	
<i>35</i>	
40	
45	
50	

	Function	xanthine permease	2,5-diketo-D-gluconic acid reductase			50S ribosomal protein L27	50S ribosomal protein L21	ribonuclease E				hypothetical protein	transposase (insertion sequence IS31831)	hypothetical protein	hypothetical protein	nucleoside diphosphate kinase		hypothetical protein	hypothetical protein	hypothetical protein
	Matched length (a.a.)	422	276			81	101	986				195	436	117	143	134		92	112	118
	Simitarity (%)	77.3	81.9			92.6	82.2	9.95				82.6	100.0	76 9	8.79	9.68		67.4	64.3	68.6
:	Identity (%)	39.1	61.2			80.3	56.4	30.1				61.0	99.1	51.3	37.8	70.9		34.8	36.6	33.9
Table 1 (continued)	Homologous gene	Bacillus subtilis 168 pbuX	Corynebacterium sp. ATCC 31090			Streptomyces griseus IFO13189 rpmA	Streptomyces griseus iFO13189 obg	Escherichia coli K12 rne	33,3			Streptomyces coelicolor A3(2) SCF76.08c	Corynebacterium glutamicum ATCC 31831	Streptomyces coelicolor A3(2) SCF76.08c	Streptomyces coelicolor A3(2) SCF76.09	Mycobacterium smegmatis ndk		Deinococcus radiodurans R1 DR1844	Mycobacterium tuberculosis H37Rv Rv1883c	Mycobacterium tuberculosis H37Rv Rv2446c
	db Match	sp. PBUX_BACSU				sp:RL27_STRGR	prt.2304263A	sp.RNE_ECOLI				gp:SCF76_8	pir:S43613	gp:SCF76_8	gp:SCF76_9	gp. AF069544_1		gp:AE002024_10	pir.H70515	pir.E70863
	ORF (bp)	1887	843	621	396	264	303	2268	549	573	747	609	1308	378	450	408	360	342	465	423
	Terminal (nt)	2501669	2501735	2503355	2504265	2503984	2504300	2504831	2507663	2507710	2508840	2509530	2509523	2511423	2511876	2511949	2512409	2513144	2513154	2513692
	Initial (nt)	2499783		2502735	2503870	2504247	2504602	2507098	2507115	2507138	2508094	2508922	2510830	2511046	2511427	2512356	2512768	25,12803	2513618	2603 6103 2514114
	SEQ NO	6085	9809	6087	6088	6089	0609	1609	6092	6093	6094	9609	9609	6097	8609	6609	6100	6101	6102	6103
	SEQ			2587	2588		2590	2591	2592	2593	2594		2596	2597	2598	2599	2600	2601	2602	2603

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

	Function	folyl-polyglutamate synthetase				valyl-tRNA synthetase	oligopeptide ABC transport system substrate-binding protein	heat shock protein dnaK	lysine decarboxylase	malate dehydrogenase	transcriptional regulator	hypothetical protein	vanillate demethylase (oxygenase)	pentachlorophenol 4- monooxygenase reductase	transport protein	malonale transporter	class-III heat-shock protein or ATP. dependent protease	hypothetical protein	succinyl CoA:3-oxoadipate CoA transferase beta subunit	succinyl CoA 3-oxoadipate CoA transferase alpha subunit
	Matched length (a.a.)	451				915	521	508	170	319	207	208	357	338	444	286	430	366	210	251
	Similarity (%)	9.67				72.1	58.5	54.9	71.2	76.5	56.5	51.4	9.89	59.2	76.8	58.4	85.8	73.0	85.7	84.5
	Identity (%)	55.4				45.5	24.2	26.2	42.9	56.4	24.6	26.0	39.5	32.8	40.8	28.0	59.8	45.6	63.3	60.2
Table 1 (continued)	Homologous gene	Streptomyces coelicolor A3(2) folC				Bacillus subtilis 168 balS	Bacillus subtilis 168 oppA	Bacillus subtilis 168 dnaK	Eikenella corrodens ATCC 23824	Thermus aquaticus ATCC 33923 mdh	Streptomyces coelicolor A3(2) Streptomyces coelicolor A3(2) SC4A10.33	Vibrio cholerae aphA	Acinetobacter sp. vanA	Sphingomonas flava ATCC 39723 pcpD	Acinetobacter sp. vanK	Klebsiella pneumoniae mdcF	Bacillus subtilis clpX	Streptomyces coelicolor A3(2) SCF55.28c	Streptomyces sp. 2065 pcaJ	Streptomyces sp. 2065 pcal
	db Match	prf.2410252B				sp:SYV_BACSU	pir.A38447	sp.DNAK_BACSU	gp:ECU89166_1	sp:MOH_THEFL	gp:SC4A10_33	gp. AF065442_1	prf.2513416F	gp:FSU12290_2	prf.2513416G	gp:KPU95087_7	prf.2303274A	gp:SCF55_28	gp.AF109386_2	gp:AF109386_1
	ORF (bp)	1374	612	714	663	2700	1575	1452	585	984	777	576	1128	975	1425	930	1278	1086	633	750
	Terminal (nt)	2514114	2516273	2516956	2517751	2515637	2518398	2521660	2521667	2522265	2524337	2524340	2526226	2527207	2528559	2528551	2529484	2531976	2531969	2532604
	Initial (nt)	2515487	2515662	2516243	2517089	2518336	2519972	2520209	2522251	2523248	2523561	2524915	2525099	2526233	2527135	2529480	2530761	2530891	2532601	2533353
	SEQ NO. (a.a.)	6104	6105	6106	6107	6108	6109	6110	6111	6112	6113	6114	6115	6116	6117	6118	6119	6120	6121	6122
	SEQ NO. (DNA)	2604	2605	2606	2607	2608	2609	2610	2611	2612	2613	2614	2615	2616	2617	2618	2619	2620	2621	2622

Table 1 (continued)

	Function	protocatechuate catabolic protein	beta-ketothiolase		3-oxoadipate enol-lactone hydrolase and 4-carboxymuconolactone decarboxylase	transcriptional regulator	3-oxoadipate enol-lactone hydrolase and 4-carboxymuconolactone decarboxylase		3-carboxy-cis, cis-muconate cycloisomerase	protocatechuate dioxygenase alpha subunit	protocatechuate dioxygenase beta subunit	hypothetical protein	muconolactone isomerase		muconate cycloisomerase		catechol 1,2-dioxygenase		toluate 1,2 dioxygenase subunit
	Matched length (a.a.)	251	406		256	825	115		437	214	217	273	92		372		285		437
	Similarity (%)	82.5	71.9		76.6	43.0	9.68		63.4	9.07	91.2	48.7	81.5		84.7		88.4		85 6
	Identity (%)	58.2	44.8		50.8	23.6	78.3		39.8	49.5	74.7	26.4	54.4		6.09		72.3		62.2
lable i (collinged)	Homologous gene	Rhodococcus opacus 1CP pcaR	Raistonia eutropha bktB		Rhodococcus opacus pcal.	Streptomyces coelicolor A3(2) SCM1.10	Rhodococcus opacus pcal.		Rhodococcus opacus pcaB	Rhodococcus opacus pcaG	Rhodococcus opacus pcaH	Mycobacterium tuberculosis H37Rv Rv0336	Mycobacterium tuberculosis catC		Rhodococcus opacus 1CP catB		Rhodococcus rhodochrous catA		Pseudomonas putida plasmid pDK1 xyIX
	db Match	prf.2408324F	prf 2411305D		prf.2408324E	gp:SCM1_10	prf.2408324E		prf.2408324D	prf.2408324C	prf.2408324B	pir.G70506	prf.2515333B		sp.CATB_RHOOP		prf.2503218A		gp.AF134348_1
	ORF (bp)	792	1224	912	753	2061	366	678	1116	612	069	1164	291	771	1119	909	855	141	1470
	Terminal (nt)	2534182	2535424	2534257	2536182	2538256	2538248	2540230	2538616	2539709	2540335	2541187	2542512	2543813	2542818	2544867	2544022	2544928	2546784
	Initral (nt)	2533391	2534201	2535168	2535430	2536196	2538613	2539553	2539731	2540320	2541024	2542350	2542802	2543043	2543936	2544262	2544876	2545068	2545315
	SEQ NO. (a.a.)	6123	6124	6125	6126	6127	6128	6129	6130	6131	6132	6133	6134	6135	6136	6137	6138	6139	6140
	SEQ NO. (DNA)	2623	2624	2625	2626	2627	2628	2629	2630	2631	2632	2633	2634	2635	2636	2637	2638	2639	2640

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

	Function	toluate 1,2 dioxygenase subunit	toluate 1,2 dioxygenase subunit	1,2-dihydroxycyclohexa-3,5-diene carboxylate dehydrogenase	regulator of LuxR famity with ATP binding site	transmembrane transport protein 4-hydroxybenzoale transporter	benzoate membrane transport protein	ATP-dependent Clp protease proteolytic subunit 2	ATP-dependent CIp protease proteolytic subunit 1	hypothetical protein	trigger factor (prolyl isomerase) (chaperone protein)	hypothetical protein	penicillin-binding protein	hypothetical protein		transposase		hypothetical protein	transposase
	Matched length (a.a.)	161	342	277	979	435	388	197	198	42	417	160	336	115		142		35	75
	Similarity (%)	83.2	81.0	61.4	48.6	64.4	66.2	88.3	85.9	71.4	66.4	63.1	50.9	58.3		73.2		82.9	787
	Identity (%)	60.3	51.5	30.7	23.3	31.3	29.9	69.5	62.1	42.9	32.1	32.5	25.3	27.8		54.2		57.1	50.7
Table 1 (continued)	Homologous gene	Pseudomonas putida plasmid pDK1 xylY	Pseudomonas putida plasmid pDK1 xylZ	Pseudomonas putida plasmid pDK1 xylL	Rhodococcus erythropolis thcG	Acinetobacter calcoaceticus pcaK	Acinetobacter calcoaceticus benE	Streptomyces coelicolor M145 clpP2	Streptomyces coelicolor M145 clpP1	Sulfolobus islandicus ORF154	Bacillus subtilis 168 tig .	Streptomyces coelicolor A3(2) SCD25.17	Nocardia lactamdurans LC411 pbp	Mus musculus Moa1		Corynebacterium striatum ORF1		Corynebacterium striatum ORF1	Corynebacterium striatum ORF1
	db Match	gp.AF134348_2	gp:AF134348_3	gp:AF134348_4	gp:REU95170_1	sp.PCAK_ACICA	sp:BENE_ACICA	gp.AF071885_2	gp.AF071885_1	gp:SIS243537_4	sp:TiG_BACSU	gp:SCD25_17	sp:PBP4_NOCLA	prf 2301342A		prf.2513302C		pri.2513302C	prf.2513302C
	ORF (bp)	492	1536	828	2685	1380	1242	624	603	150	1347	495	975	456	249	438	150	126	264
	Terminal (nt)	2547318	2548868	2549695	2552455	2553942	2555267	2555317	2555978	2556748	2556760	2559103	2560131	2560586	2561363	2561483	2562242	2561990	2562078
	Initial (nt)	2546827	2547333	2548868	2549771	2552563	2554026	2555940	2556580	2556599	2558106	2558609	2559157	2560131	2561115	2561920	2562093	2562115	2562341
	SEQ NO (a a.)	6141	6142	6143	6144	6145	6146	6147	6148	6149	6150	6151	6152	6153	6154	6155	6156	6157	6158
	SEQ NO.	2641	2642	2643	2644	2645	2646	2647	2648	2649	2650	2651	2652	2653	2654	2655	2656	2657	2658

Table 1 (continued)

						(Sommers) a signi				
SEQ NO (DNA)	SEQ NO.	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched length (a a)	Function
2659	6159	2562776	2562387	390						
2660	6160	2562963	2563847	885						
2661	6161	2564402	2563932	471	sp.LACB_STAAU	Staphylococcus aureus NCTC 8325-4 tacB	40.0	71.4	140	galactose-6-phosphate isomerase
2992	6162	2565245	2564550	969	Sp.YAMY_BACAD	Bacillus acidopullulyticus ORF2	26.2	58.1	248	hypothetical protein
2663	6163	2566231	2565623	609	pir.A70866	Mycobacterium tuberculosis H37Rv Rv2466c	56.8	6.08	199	hypothetical protein
2664	6164	2566345	2568945	2601	SP. AMPN_STRLI	Streptomyces lividans pepN	47.5	70.5	890	aminopeptidase N
2665	6165	2569211	2570293	1083	pir:B70206	Borrelia burgdorferi BB0852	25.1	58.1	358	hypothetical protein
2666	9919	2571460	2570309	1152						
2667	6167	2571510	2572175	999						
2668	6168	2572193	2572348	156						
2669	6169	2572677	2572351	327	gp:AF139916_3	Brevibacterium linens ATCC 9175 ctl 9175 ctl	61.5	81.7	104	phytoene desaturase
2670	6170	2572977	2572807	171						
2671	6171	2573770	2573393	378						
2672	6172	2573864	2572659	1206	sp.CRTJ_MYXXA	Myxococcus xanthus DK1050 carA2	31.2	63.8	381	phytoene dehydrogenase
2673	6173	2574718	2573843	876	sp.CRTB_STRGR	Streptomyces griseus JA3933 cr18	31.4	58.6	290	phytoene synthase
2674	6174	2575898	2574780	1119	gp:LMAJ9627_3	Listeria monocytogenes lltB	25.8	47.7	392	multidrug resistance transporter
2675	6175	2577213	2575981	1233						
2676	6176	2578872	2577232	1641	gp:SYOATPBP_2	Synechococcus elongatus	41.3	71.6	538	ABC transporter ATP-binding protein
2677	6177	2579760	2578879	882	sp:DPPC_BACFI	Bacillus firmus OF4 dppC	38.8	73.8	286	dipeptide transport system permease protein
2678	6178	2580707	2579769	939	pir.S47696	Escherichia coli K12 nikB	33.2	62.0	316	nickel transport system permease protein
2679	6179	2582417	2580711	1707						

						Table 1 (continued)				
SEQ NO.	SEQ NO (a a)	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	. Homologous gene	Identity (%)	Similarity (%)	Matched length (a a)	Function
2680	6180	2582564	2584504	1941		•				
2681	6181	2584613	2585926	1314	sp:ARGD_CORGL	Corynebacterium glutamicum ATCC 13032 argD	31.4	63 5	411	acetylornithine aminotransferase
2682	6182	2586180	2587763	1584	pir:A70539	Mycobacterium tuberculosis H37Rv Rv1128c	25.1	47.9	482	hypothetical protein
2683	6183	2587976	2588722	747	sp:YA26_MYCTU	Mycobacterium tuberculosis H37Rv Rv0364	49.1	79.4	218	hypothetical membrane protein
2684	6184	2589432	2588725	708	sp:PHBB_CHRVI	Chromatium vinosum D phbB	28.1	0 09	235	acetoacetyl CoA reductase
2685	6185	2589565	2590302	738	pir.A40046	Streptomyces coelicolor actil	26.7	55.0	240	transcriptional regulator, TetR family
2686	6186	2590697	2591137	441	GSP:Y74375	Neisseria meningitidis	38.0	47.0	94	polypeptides predicted to be useful antigens for vaccines and diagnostics
2687	6187	2592365	2591574	792	gp:AF106002_1	Pseudomonas putida GM73 ttg2A	31.1	65.1	238	ABC transporter ATP-binding protein
2688	6188	2592402	2592794	393	gp:MLCB1610_9	Mycobacterium leprae MLCB1610.14c	53.2	77.0	126	globin
2689	6189	2592838	2593965	1128	sp.CHRA_PSEAE	Pseudomonas aeruginosa Plasmid pUM505 chrA	27.3	60.4	396	chromate transport protein
2690	6190	2594594	2593968	627	pir.A70867	Mycobacterium tuberculosis H37Rv Rv2474c	37.8	68.9	196	hypothetical protein
2691	6191	2595061	2594597	465	gp:SC6D10_19	Streptomyces coelicolor A3(2) SC6D10.19c	36.2	61.4	127	hypothetical prolein
2692	6192	2595808	2595188	621						
2693	6193	2595983	2595652	162	pir.B72589	Aeropyrum pernix K1 APE1182	36.4	0.09	55	hypothetical protein
2694	6194	2597715	2596048	1668	sp:YJJK_ECOLI	Escherichia coli K12 yijK	52.8	9.62	563	ABC transporter ATP-binding protein
2695	6195	2598483	2597869	615	pir.E70867	Mycobacterium tuberculosis H37Rv Rv2478c	31.4	62.2	172	hypothetical protein
2696	6196	2600764	2598662	2103	sp:Y05L_MYCLE	Mycobacterium leprae o659	28.0	26.7	700	hypothetical membrane protein
2697	6197	2601461	2602879	1419	pir.C69676	Bacillus subtilis phoB	28.0	52.6	536	alkaline phosphatase

	Function			multiple sugar-binding transport system permease protein	multiple sugar-binding transport system permease protein		maltose-binding protein		ABC transporter ATP-binding protein (ABC-type sugar transport protein) or cellobiose/maltose transport protein			dolichol phosphate mannose synthase		aldehyde dehydrogenase	circadian phase modifier		hypothetical membrane protein	glyoxylate-induced protein	ketoacyl reductase	oligoribonuclease
	Matched length (a.a.)			279	292		462		386			154		207	183		412	255	258	179
ļ	Similarity (%)			76.3	67.5		63.2		79.8			72.7		89.4	73.8		64.6	69.4	0.78	78.8
	Identity (%)			39.1	27.4		28.8		59.1			37.7		67.2	48.6		35.0	41.2	40.0	48.0
Table 1 (continued)	Homologous gene			Streptococcus mutans INGBRITT msmG	Streptococcus mutans INGBRITT msmF		Thermoanaerobacterium thermosul amyE		Streptomyces reticuli msiK			Schizosaccharomyces pombe dpm1	•	Rhodococcus rhodochrous plasmid pRTL1 orf5	Synechococcus sp. PCC7942 cpmA		Thermotoga maritima MSB8 TM0964	Escherichia coli K12 gip	Mycobacterium tuberculosis H37Rv Rv1544	Escherichia coli K12 orn
	db Match			SP.MSMG_STRMU	sp:MSMF_STRMU		pri.2206392C		prf.2308356A			prf.2317468A		prf 2516398E	prf.2513418A		pir.A72312	sp:GIP_ECOLI	pir.E70761	sp:ORN_ECOLI
	ORF (bp)	930	639	912	843	1674	1329	1242	1128	- 200	02/	684	069	789	762	345	1182	750	798	657
-	Terminal (nt)	2605502	2603945	2604609	2605527	2608117	2606561	2608185	2609512	000000	7/77197	2610848	2613151	2614500	2615410	2615795	2615939	2617995	2618869	2619538
	Initial (nt)	2604573	2604583	2605520	2606369	2606444	2607889	2609426	2610639	90000	2611523	2611531	2612462	2613712	2614649	2615451	2617120	2617246	2618072	2618882
	SEQ NO. (a.a.)	6198	6199	6200	6201	6202	6203	6204	6205	4000	9079	6207	6208	6209	6210	6211	6212	6213	6214	6215
	SEQ NO. (DNA)	2698	2699	2700	2701	2702	2703	2704	2705		2/06	2707	2708	2709	2710.	2711	2712	2713	2714	2715

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

$\overline{}$
豆
a
_
_
.=
-
_
0
Ö
_
<del></del>
a)
_
ρ
=
୍ଟ
$\vdash$

_	<del>-</del> -							<del></del>			<del></del> -									
	Function	ferric enterochelin esterase	lipaprotein				transposase (IS1207)			transcriptional regulator	glutaminase	sporulation-specific degradation regulator protein		uronate isomerase		hypothetical protein	pyrazinamidase/nicotinamidase	hypothetical protein	bacterioferritin comigratory protein	bacterial regulatory protein, tetR family
	Matched length (a a)	454	398				436			131	358	97		335		291	185	75	141	114
	Identity Similarity (%)	50.9	71.9				8.66			63.4	69.3	72.2		6.09		45.0	74.6	0.08	73.8	61.4
	Identity (%)	26.0	48.5				99.5			32.8	35.2	42.3		29.0		32.0	48.1	42.7	46.8	32.5
Table 1 (continued)	Homologous gene	Salmonella enterica iroD	Mycobacterium tuberculosis H37Rv Rv2518c IppS				Corynebacterium glutamicum ATCC 21086			Salmonella typhimurium KP1001 cytR	Rattus norvegicus SPRAGUE- BAWLEЎ KIBNEЎ	Bacillus subtilis 168 degA		Escherichia coli K12 uxaC		Zea diploperennis perennial teosinte	Mycobacterium avium pncA	Mycobacterium tuberculosis H37Rv Rv2520c	Escherichia coli K12 bcp	Streptomyces coelicolor A3(2) SC111.01c
	db Match	prf.2409378A	pir:C70870				gp.SCU53587_1			gp:AF085239_1	sp.GLSK_RAT	pir.A36940		sp:uxAc_Ecoti		prf.1814452C	prf.232444A	pir E70870	sp:BCP_ECOLI	gp:SCI11_1
i	ORF (bp)	1188	1209	645	150	246	1308	207	639	453	1629	477	555	1554	501	1197	558	273	465	636
	Terminal (nt)	2619541	2620973	2623605	2623621	2624048	2624051	2625806	2625809	2628376	2626493	2628852	2628324	2630479	2631136	2632466	2633100	2633146	2634064	2634751
	Initial (nt)	2620728	2622181	2622961	2623770	2623803	2625358	2625600	2626447	2627924	2628121	2628376	2628878	2628926	2630636	2631270	2632543	2633418	2633600	2634116
	SEQ NO. (a.a.)	6216	6217	6218	6219	6220	6221	6222	6223	6224	6225	6226	6227	6228	6229	6230	6231	6232	6233	6234
	SEQ NO (DNA)	2716	2717	2718	2719	2720	2721	2722	2723	2724	2725	2726	2727	2728	2729	2730	2731	2732	2733	2734

5	
10	
15	
20	
25	
30	
35	
40	
45	

	Function	phosphopantethiene protein transferase	lincomycin resistance protein	hypothetical membrane protein		fatty-acid synthase	hypothetical protein	peptidase	hypothetical membrane protein	hypothetical membrane protein	hypothetical protein	ribonuclease PH				hypothetical membrane protein	transposase (IS1628)		arylsulfatase
	Matched length (a.a.)	145	473	113		3029	404	230	112	113	202	236				428	175		250
	Similarity (%)	75.9	85 6	54.0		836	55.2	6.09	6 29	0.69	7.97	814				58.2	2.79		74.4
	Identity (%)	56.6	52.4	30.1		62.3	25.3	40.4	40.2	37.2	55.0	60.2				29.0	92.1		46.0
Table 1 (continued)	Homologous gene	Corynebacterium ammoniagenes ATCC 6871 ppt1	Corynebacterium glutamicum ImrB	Synechocystis sp. PCC6803		Corynebacterium ammoniagenes fas	Streptomyces coelicolor A3(2) SC4A7.14	Mycobacterium tuberculosis H37Rv Rv0950c	Mycobacterium tuberculosis H37Rv Rv1343c	Mycobacterium leprae B1549_F2_59	Mycobacterium tuberculosis H37Rv Rv1341	Pseudomonas aeruginosa ATCC 15692 rph				Mycobacterium tuberculosis H37Rv SC8A6.09c	Corynebacterium glutamicum 22243 R-plasmid pAG1 tnpB		Mycobacterium leprae ats
	db Match	gp:BAY15081_1	gp.AF237667_1	pir.S76537		pir:S2047	gp:SC4A7_14	pir:D70716	sp:Y077_MYCT	sp:Y076_MYCLE	sp. Y03Q_MYCTU	sp:RNPH_PSEAE				sp:Y029_MYCTU	gp:AF121000_8		sp:Y03O_MYCLE
	ORF (bp)	405	1425	324	414	8979	1182	615	462	354	618	735	246	693	582	1362	534	099	765
	Terminal (nt)	2634747	2635165	2637168	2637240	2638649	2648235	2650164	2650902	2651339	2651420	2652067	2653009	2653326	2654079	2654875	2656985	2656974	2657736
	Initial (nt)	2635151	2636589	2636845	2637653	2647627	2649416	2649550	2650441	2650986	2652037	2652801	2653254	2654018	2654660	2656236	2656452	2657633	2658500
	SEQ NO (a a.)	6235	6236	6237	6238	6239	6240	6241	6242	6243	6244	6245	6246	6247	6248	6249	6250	6251	6252
	SEQ NO (DNA)	2735	2736	2737	2738	2739	2740	2741	2742	2743	2744	2745	2746	2747	2748	2749	2750	2751	2752

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

	Function	ribonucleolide reductase beta-chain	ferritin	sporulation transcription factor	iron dependent repressor or diptheria toxin repressor	cold shock protein TIR2 precursor	hypothetical membrane protein	ribonucleotide reductase alpha- chain	•	50S ribosomal protein L36	NH3-dependent NAD(+) synthetase			hypothetical protein	hypothetical protein	alcohol dehydrogenase	Bacillus subtilis mmg (for mother cell metabolic genes)	hypothetical protein		phosphoglucomulase
	Matched length (a a)	334	159	256	225	124	50	707		41	279			257	96	337	459	284		556
	Similarity (%)	99.7	64.2	60.2	60.4	62.1	0.98	100.0		79.0	78.1			56.4	68.8	52.8	56.0	66.2		90.6
	Identity (%)	99.7	31.5	32.8	27.6	24 2	20.0	6:66		0.85	55.6			30.7	41.7	26.1	27.0	33.8		61.7
Table 1 (continued)	Homologous gene	Corynebacterium glutamicum ATCC 13032 nrdF	Escherichia coli K12 finA	Streptomyces coelicolor A3(2) whiH	Corynebacterium glutamicum ATCC 13869 dtxR	Saccharomyces cerevisiae YPH148 YOR010C TIR2	Archaeoglobus fulgidus AF0251	Corynebacterium glutamicum ATCC 13032 nrdE		Rickettsia prowazekii	Bacillus subtilis 168 nadE			Synechocystis sp. PCC6803 sir1563	Mycobacterium tuberculosis H37Rv Rv3129	Bacillus stearothermophilus DSM 2334 adh	Bacillus subtilis 168 mmgE	Arabidopsis thaliana T6K22.50		Escherichia coli K12 pgm
	db Match	gp:AF112536_1	sp.FTNA_ECOLI	gp.SCA32WHIH_4	pir:140339	sp.TIR2_YEAST	pir:C69281	gp:AF112535_3		SP:RL36_RICPR	sp:NADE_BACSU			pir.S76790	pir.G70922	sp.ADH2_BACST	sp:MMGE_BACSU	pir:T05174		sp.PGMU_ECOLI
	ORF (bp)	1002	486	750	099	438	276	2121	315	<del>2</del>	831	93	498	747	288	1020	1371	834	792	1662
	Terminal (nt)	2673338	2675289	2676240	2676243	2677377	2676918	2677478	2680784	2681223	2682376	2681464	2683616	2682379	2683131	2683627	2686289	2687148	2687449	2688389
	Initial (nt)	2674339	2674804	2675491	2676902	2676940	2677193	2679598	2680470	2681363	2681546	2681556	2683119	2683125	2683418	2684646	2684919	2686315	2688240	2690050
	SEQ NO (a.a.)	6271	6272	6273	6274	6275	6276	6277	6278	6279	6280	6281	6282		6284	6285	6286	6287	6288	6289
	SEQ NO (DNA)	2771	2772	2773	2774	2775	2776	2777	2778	2779	2780	2781	2782	2783	2784	2785	2786	2787	2788	2789

**5** 

							Table 1 (continued)				
0 2 3	SEQ NO. (DNA)	SEQ NO. (a a.)	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched length (a.a.)	Function
2	2790	6290	2690150	2690437	288	pir.F70650	Mycobacterium tuberculosis H37Rv Rv3069	41.7	64.3	84	hypothetical membrane protein
_ 7	2791	6291	2690437	2690760	324	pir:D71843	Helicobacter pylori J99 jhp1146	25 4	61.5	122	hypothetical membrane protein
7	2792	6292	2690773	2691564	792	sp.YCSI_BACSU	Bacillus subtilis 168 ycsl	512	79.1	254	hypothetical protein
2	2793	6293	2691689	2693053	1365	gp. AF126281_1	Rhodococcus erythropolis	24.2	486	496	(IS1676)
2	2794	6294	6294 2693299	2694918	1620	sp.CSP1_CORGL	Corynebacterium glutamicum (Brevibacterium flavum) ATCC 17965 csp1	24.8	49.6	355	major secreted protein PS1 protein precursor
2	2795	6295	2694926	2695279	354						
2	2796	6296	6296 2695554	2695718	165					!	
2	2797	6297	2695766	2695320	447						
7	2798	6298	6298 2695812	2697212	1401	gp:AF126281_1	Rhodococcus erythropolis	24.6	46.6	500	transposase (IS1676)
7	2799	6299	2698150	2697383	768						
											proton/sodium-alutamate sympot
5	2800	6300	2699531	2698194	1338	sp:GLTT_BACCA	Bacillus subtilis 168	30.8	66.2	438	protein
7	2801	6301	2700920	2701612	693						
2	2802	6302	2702466	2699926	2541	gp:SCE25_30	Streptomyces coelicolor A3(2) SCE25.30	33.0	0.69	873	ABC transporter
5	2803	6303	2702466	2703356	891						
2	2804	6304	2703194	2702487	708	gp:SAU18641_2	Staphylococcus aureus	45.4	79.8	218	ABC transporter ATP-binding protein
7	2805	6305	2704314	2704586	273	PIR:F81516	Chlamydophila pneumoniae AR39 CP0987	0.09	0 29	84	hypothetical protein
7	2806	9069	2704835	2704975	141	PIR:F81737	Chlamydia muridarum Nigg TC0129	71.0	75.0	42	hypothetical protein
2	2807	6307	2709878	2710555	8/9						
2	2808	6308	6308 2710637	2711308	672	prf.2509388L	Streptomyces collinus Tu 1892 ansG	28.1	54.1	196	oxidoreductase or dehydrogenase
											The same of the sa

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

_
nued
conti
<u>ت</u>
. apple
-

_					_											_				
-	Function	methyltransferase	hypothetical protein	hypothetical protein		UDP-N-acetylglucosamine 1- carboxyvinyltransferase	hypothetical protein	transcriptional regulator		cysteine synthase	O-acetylserine synthase	hypothetical protein	succinyl-CoA synthetase alpha chain	hypothelical protein	succinyl-CoA synthetase beta chain		frenolicin gene E product		succinyl-CoA coenzyme A transferase	transcriptional regulator
	Matched length (a a)	205	84	42	.	417	190	281		305	172	83	291	75	400		213		501	321
	Similarity (%)	51.2	0.99	75.0		75.3	84.2	0 69		846	7.67	65 1	79.4	430	73.0		718		8 //	68.5
	Identity (%)	25.9	61.0	71.0		44.8	66.3	45.9		1.73	61.1	36.1	52.9	42.0	39.8		38.5		47.9	38.6
Table I (commued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv0089	Chlamydia pneumoniae	Chlamydia muridarum Nigg TC0129		Acinetobacter calcoaceticus NCIB 8250 murA	Mycobacterium tuberculósis H37Rv Rv1314c	Streptomyces coelicolor A3(2) SC2G5.15c		Bacillus subtilis 168 cysK	Azotobacter vinelandii cysE2	Deinococcus radiodurans R1 DR1844	Coxiella burnetii Nine Mile Ph I sucD	Aeropyrum pernix K1 APE1069	Bacillus subtilis 168 sucC		Streptomyces roseofulvus frnE		Clostridium kluyveri cat1 cat1	Azospirillum brasilense ATCC 29145 ntrC
	db Match	sp:Y089_MYCTU	GSP:Y35814	PIR:F81737		sp:MURA_ACICA	sp:Y02Y_MYCTU	gp:SC2G5_15		Sp.CYSK_BACSU	prf.2417357C	gp:AE002024_10	os suco coxBu	PIR:F72706	sp.SUCC_BACSU		gp:AF058302_5		Sp.CAT1_CLOKL	43 sp:NIR3_AZOBR
ì	ORF (bp)	525	273	141	195	1254	570	843	408	924	546	288	882	225	1194	360	735	819	1539	1143
	Terminal (nt)	2712374	2713453	2713842	2717993	2718436	2720319	2720385	2721295	2722857		2723770	2724478	2725843	2725384	2726786	2727399	2728207	2729378	2732518
	Initial (nt)	2711850	2713181	2713702	2718187	2719689	2719750	2721227	2721702	2721934	2723064	2724057	2725359	2725619	6322 2726577	2727145	2728133	2729025	2730916	2731376
	SEQ NO.		6310	6311	6312	6313	6314	6315	6316	6317	6318	6319	6320	6321		6323	6324	6325	6326	6327
	SEQ NO (DNA)	2809	2810	2811	2812	2813	2814	2815	2816	2817	2818	2819	2820	2821	2822	2823	2824	2825	2826	2827

		1				ŀ		- 1	1		1 1	- 1	i	į		au l	1
5		_		ystem	ınsport	port system	port system	otein S-3					o acid			minoimidazol	transferase
10		Function		phosphate transport system regulatory protein	phosphate-specific transport component	phosphate ABC transport system permease protein	phosphate ABC transport system permease protein	phosphate-binding protein S-3 precursor	acetyltransferase		hypothetical protein	hypothetical protein	branched-chain amino acid aminotransferase	hypothetical protein	hypothetical protein	5'-phosphoribosyl-5-aminoimidazole synthetase	amidophosphoribosyl transferase
15		Matched length (a a)		213	255	292	325	369	315		344	225	259	352	58	347	482
20		Similarity (%)		81.7	82.8	82.2	78.5	26.0	0.09		55.2	74.2	26.0	79.0	81.0	94.2	89.0
		Identity (%)		46.5	58.8	51.4	50.2	40.0	34.3		24.7	44.9	28.6	58.5	58.6	81.0	70.3
25	(p <sub>e</sub>			Sis	pstB	Si5	Sis	iis	3(2)			Sis	<b>t</b> 2	7.5	sis	72	72
30 35	Table 1 (continued)	Homologous gene		Mycobacterium tuberculosis H37Rv Rv0821c phoY-2	Pseudomonas aeruginosa pstB	Mycobacterium tuberculosis H37Rv Rv0830 pstA1	Mycobacterium tuberculosis H37Rv Rv0829 pstC2	Mycobacterium tuberculosis H37Rv phoS2	Streptomyces coelicolor A3(2) SCD84, 18c		Bacillus subtilis 168 bmrU	Mycobacterium tuberculosis H37Rv Rv0813c	Solanum tuberosum BCAT2	Corynebacterium ammoniagenes ATCC 6872 ORF4	Mycobacterium tuberculosis H37Rv Rv0810c	Corynebacterium ammoniagenes ATCC 6872 purM	Corynebacterium ammoniagenes ATCC 6872 purF
40		db Match		pir:E70810	pir.S68595	gp:MTPSTA1_1	pir.A70584	pir.H70583	gp:SCD84_18		SP.BMRU_BACSU	pir.E70809	gp:AF193846_1	gp:AB003158_6	pir:B70809	gp:AB003158_5	gp:AB003158_4
		ORF (bp)	807	732	897	921	1014	1125	876	783	1095	687	942	1101	213	1074	1482
45		Terminal (nt)	2731424	2733367	2733455	2734264	2735202	2736414	2737836	2739553	2739556	2741356	2741636	2743785	2744222	2744881	2746083
50		Initial (nt)	2732230	1	2734351	2735184	2736215	2737538	2738711	2738771	2740650	2740670	2742577	2742685	2744010	2745954	2747564
		SEQ NO			6330	6331	6332	6333	6334	6335	6336	6337	6338	6339	6340	6341	6342
55		SEQ NO.	2828	2829	2830	2831	2832	2833	2834	2835	2836	2837	2838	2839	2840	2841	2842

5		Function	hypothetical protein	hypothelical protein	hypothetical membrane protein	hypothetical protein	5'-phosphoribosyl-N- formylglycinamidine synthetase		5-phosphoribosyl-N- o-priosprioribosyriv- formylglycinamidine synthetase	hypothetical protein		gluthatione peroxidase	extracellular nuclease		hypothetical protein	C4-dicarboxylate transporter	dipeptidyl aminopeptidase
15		Matched length (a.a.)	124	315	217	42	763		223	62		158	965		211	414	269
20		Similarity (%)	75.8	94.0	87.1	71.0	89.5		93.3	93.7		77.9	51.5		68.7	816	9.07
		Identity (%)	57.3	75.9	67.7	64.0	77.6		80.3	81.0		46.2	28.0		37.4	49.0	41.8
25	ਉ		S	2	2		2		, i, i	.5			P636		S	12	1apb1
<i>30</i>	Table 1 (continued)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv0807	Corynebacterium ammoniagenes ATCC 6872 ORF2	Corynebacterium ammoniagenes ATCC 6872 ORF1	Sulfolobus solfataricus	Corynebacterium ammoniagenes ATCC 6872 purL		Corynebacterium ammoniagenes ATCC 6872 purQ	Corynebacterium ammoniagenes ATCC 6872 purorf		Lactococcus factis gpo	Aeromonas hydrophila JMP636 nucH		Mycobacterium tubercutosis H37Rv Rv0784	Salmonella typhimurium LT2 dctA	Pseudomonas sp. WO24 dapb1
40		db Match	pir:H70536	gp.AB003158_2	gp:AB003158_1	GP:SSU18930_21 4	gp.AB003162_3		gp.AB003162_2	gp:AB003162_1		рп.2420329А	prf.2216389A		pir.C70709	sp.DCTA_SALTY	prf.2408266A
		ORF (bp)	375	1017	741	186	2286	720	699	243	522	477	2748	276	687	1338	2118
45		Terminal (nt)	2747683	2749111	2749162	2752103	2750027	2753121	2752327	2752995	2753819	2753328	2756739	2757126	2757129	2757863	2759532
50		Initial (nt)	2748057	2748095	2749902	2751918	2752312	2752402	2752995	2753237	2753298	2753804	2753992	2756851	2757815	2759200	2761649
		SEQ NO.		6344	6345	6346	6347	6348	6349	6350	6351	6352	6353	6354	6355	6356	6357
55		SEQ NO.	2843	2844	2845	2846	2847	2848	2849	2850	2851	2852	2853	2854	2855	2856	2857

	Function		5-phosphoribosyl-4-N- succinocarboxamide-5-amino imidazole synthetase	adenylosuccino lyase	aspartate aminotransferase	5'-phosphoribosylglycınamide synthetase	histidine triad (HIT) family protein	,	hypothetical protein nypothetical protein	di-Aripeptide transpoter	adenosylmethionine-8-amino-7- oxononanoate aminotransferase or 7,8-diaminopelargonic acid aminotransferase	dethiobiotin synthetase	two-component system sensor histidine kinase	two-component system regulatory protein	transcriptional activator	metal-activated pyridoxal enzyme or low specificity D-Thr aldolase
	Matched length (a.a.)		294	477	395	425	136		243	469	423	224	335	231	249	382
	Similarity (%)		89.1	95.0	62.3	86.4	80 2		56.4 56.4	9.79	98.8	9.66	70.5	72.7	69.5	53.9
	Identity (%)		70.1	85.3	28.1	71.1	53.7		8.92	30.1	95.7	98.7	31.3	42.0	37.4	30.9
Table 1 (continued)	Homologous gene		Corynebacterium ammoniagenes ATCC 6872 purC	Corynebacterium ammoniagenes ATCC 6872 purB	Sulfolobus solfataricus ATCC 49255	Corynebacterium ammoniagenes ATCC 6872 purD	Mycobacterium leprae u296a		Methanosarcina barkeri orf3 Methanosarcina barkeri orf3	Lactococcus lactis subsp. lactis dipT	Corynebacterium glutamicum (Brevibacterium flavum) MJ233 bioA	Corynebacterium glutamicum (Brevibacterium flavum) MJ233 bioD	Lactococcus lactis M71plasmid pND306	Thermotoga maritima drrA	Streptomyces lividans tipA	Arthrobacter sp. DK-38
•	db Match		gp:AB003161_3	gp.AB003161_2	sp:AAT_SULSO	gp:AB003161_1	Sp:YHIT_MYCLE		pir: §82195	sp.DTPT_LACLA	1269 sp.BIOA_CORGL	sp.BIOD_CORGL	gp:AF049873_3	prf:2222216A	sp TIPA_STRL1	prf.2419350A
	ORF (bp)	624	891	1428	1158	1263	414	435	753	1356	1269	672	1455	705	753	1140
,	Terminal (nt)	2761829	2761785	2763504	2764978	2766158	2767993	2767703	3768343	2769156	2771982	2772660	2772644	2774110	2774937	2775740
	Initial (nt)	2762452	2762675	2764931	2766135	2767420	2767580	2768137	2789895	2770511	2770714	2771989	2774098	2774814	2775689	2776879
	SEQ NO.	6358	6329	6360	6361	6362	6363	6364	6365	9969	6367	6368	6369	6370	6371	6372
	SEO NO (DNA)	2858	2859	2860	2861	2862	2863	2864	2865	2866	2867	2868	2869	2870	2871	2872

5
10
15
20
25
30
35
40
45
50

Table 1 (continued)

	Function	ABC transporter	hypothetical membrane protein	transposase (ISA0963-5)		3-kelosteroid dehydrogenase		Ipopolysaccharide biosynthesis protein or oxidoreductase or dehydrogenase	dehydrogenase or myo-inositol 2- dehydrogenase	shikimate transport protein	shikimate transport protein	transcriptional regulator	ribosomal RNA ribose methylase or IRNA/rRNA methyltransferase	cysteinyl-tRNA synthetase	PTS system, enzyme II sucrose protein (sucrose-specific IIABC component)	sucrose 6-phosphate hydrolase or sucrase	glucosamine-6-phosphate isomerase	N-acetylglucosamine-6-phosphate deacetylase
	Matched length (a a)	223	135	303		561		204	128	292	130	212	334	464	. 899	473	248	368
	Similarity (%)	63.2	87.4	52.5		62 0		56.4	69.5	67.5	80.8	55.7	47.3	68.8	77.0	56.9	69.4	60 3
	Identity (%)	31.4	0.09	23.4		32.1		34.3	35.2	30.5	43.1	32.6	22.8	42.2	47.0	35.3	38.3	30 2
I anie i (commuteu)	Homologous gene	Staphylococcus aureus 8325-4 mreA	Mycobacterium tuberculosis H37Rv Rv2060	Archaeoglobus fulgidus		Rhodococcus erythropolis SQ1 kstD1		Thermotoga maritima MSB8 bpIA	Bacillus subtilis 168 idh or iolG	Escherichia coli K12 shiA	Escherichia coli K12 shiA	Streptomyces coelicolor A3(2) SC5A7.19c	Saccharomyces cerevisiae YOR201C PET56	Escherichia coli K12 cysS	Lactococcus laclis sacB	Clostridium acetobutylicum ATCC 824 scrB	Escherichia coli K12 nagB	Vibrio furnissii SR1514 manD
	db Match	gp:AF121672_2	pir.E70507	pir:A69426		gp:AF096929_2		pir.B72359	sp:MI2D_BACSU	sp. SHIA_ECOLI	sp.SHIA_ECOLI	gp:SC5A7_19	sp. PT56_YEAST	sp:SYC_ECOLI	prf.2511335C	gp:AF205034_4	sp:NAGB_ECOLI	52 sp.NAGA_VIBFU
	ORF (bp)	069	555	1500	201	1689	747	618	435	855	426	654	939	1380	1983	1299	759	1152
	Terminal (nt)	2798509	2799391	2801034	2801313	2801558	2803250	2804074	2804676	2805113	2806016	2806599	2807426	2808399	2809824	2811960	2813279	2814081
	Initial (nt)	2797820	2798837	2799535	2801113	2803246	2803996	2804691	2805110	2805967	2806441	2807252	2808364	2809778	2811806	2813258	2814037	2815232
	SEQ NO (a.a)	6391	6392	6393	6394	6395	9629	6397	6398	6389	6400	6401	6402	6403	6404	6405	6406	6407
	SEQ NO (DNA)	2891	2892	2893	2894	2895	2896	2897	2898	2899	2900	2901	2905	2903	2904	2905	2906	2907

5
10
15
20
25
30
35
40
45
50

	Function	dihydrodipicolinate synthase	glucokinase	N-acetylmannosamine-6-phosphate epimerase		sialidase precursor	L-asparagine permease operon repressor	dipeptide transporter protein or heme-binding protein	dipeptide transport system permease protein	olinonentide transport ATP-binding protein	oligopeptide transport ATP-binding protein	homoserine/homoserin lactone efflux protein or lysE type translocator	leucine-responsive regulatory protein		hypothetical protein	hypothetical protein	transcription factor
	Matched length (a a)	298	321	220		439	222	260	342	314	258	193	142		152	235	157
	Similarity (%)	62 1	57.6	68.6		50.3	57.2	51.4	64.3	78.3	7.87	62.7	66.2		86 2	71.5.	91.1
	identity (%)	28.2	28.7	36.4		24.8	26.6	22.5	31.9	46.5	43.4	28.5	31.0		55.9	46.4	73.3
Table 1 (continued)	Homologous gene	Escherichia coli K12 dapA	Streptomyces coelicolor A3(2) SC6E10.20c glk	Clostridium perfringens NCTC 8798 nanE		Micromonospora viridifaciens ATCC 31146 nadA	Rhizobium etti ansR	Bacillus firmus OF4 dppA	Bacillus firmus OF4 dappB	Bacillus subtilis 168 oppD	Lactococcus lactis oppF	Escherichia coli K12 rhtB	Bradyrhizobium japonicum Irp		Mycobacterium tuberculosis H37Rv Rv3581c	Mycobacterium tuberculosis H37Rv Rv3582c	Mycobacterium tuberculosis H37Rv Rv3583c
	db Match	sp. DAPA_ECOLI	sp.GLK_STRCO	prf.2516292A		sp:NANH_MICVI	gp:AF181498_1	gp:BFU64514_1	sp.DPPB_BACFI	sp:OPPD_BACSU	sp:OPPF_LACLA	sp:RHTB_ECOLI	prf.2309303A		pir.C70607	sp:Y18T_MYCTU	pir H70803
	ORF (bp)	936	606	969	177	1215	729	1608	951	1068	816	621	483	360	480	768	594
	Terminal (nt)	2816393	2817317	2818058	2818137	2818350	2819557	2822191	2823337	2825341	2826156	2826215	2827404	2827458	2827904	2828379	2829156
	Initial (nt)	2815458	2816409	2817363	2818313	2819564	2820285	2820584	2822387	2824274	2825341	2826835	2826922	2827817	2828383	2829146	2829749
	SEQ NO (a a )	6408	6409	6410	6411	6412	6413	6414	6415	6416	6417	6418	6419	6420	6421	6422	6423
	SEQ NO.	2908	2909	2910	2911	2912	2913	2914	2915	2916	2917	2918	2919	2920	2921	2922	2923

Table 1 (continued)

.

SEQ NO DNA)	SEQ NO.	Initial (nt).	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched length (a a)	Function
2924		2830057	2830779	723	prf.2214304A	Mycobacterium tuberculosis H37Rv Rv3246c mtrA	43.5	70.0	223	two-component system response regulator
2925	6425	2830779	2831894	1116	sp.BAES_ECOLI	Escherichia coli K12 baeS	29.3	67.7	341	two-component system sensòr histidine kinase
2926	6426	2832085	2832666	582						
2927	6427	2832790	2834181	1392	sp.RADA_ECOLI	Escherichia coli K12 radA	41.5	74.3	463	DNA repair protein RadA
2928	6428	2834188	2835285	1098	sp.YACK_BACSU	Bacillus subtilis 168 yacK	40.3	73.3	345	hypothetical protein
2929	6429	2835969	2835283	687	pir D70804	Mycobacterium tuberculosis H37Rv Rv3587c	29.4	53.3	231	hypothetical protein
2930	6430	2837499	2836048	1452	gp.PPU96338_1	Pseudomonas putida NCIMB 9866 plasmid pRA4000	59.5	85.1	471	p-hydroxybenzaldehyde dehydrogenase
2931	6431	2837737	2837591	147						
2932	6432		2837956	621	621 pir T08204	Chlamydomonas reinhardtii ca1	36.7	66.2	210	mitochondrial carbonate dehydratase beta
2933	6433	2838643	2839521	879	gp.AF121797_1	Streptomyces antibioticus IMRU 3720 mutY	48.4	7.07	283	A/G-specific adenine glycosylase
2934	6434	2839562	2840716~	1155						
2935	6435	2841063	2840758	306						
2936		6436 2841075	2841848	774	gp:AB009078_1	Brevibacterium saccharolyticum	99.2	9 66	258	L-2.3-butanediol dehydrogenase
2937		6437 2842130	2842453	324				-		
2938		6438 2842493	2843233	741						
2939		6439 2843405	2843716	312						
2940	6440	6440 2843722	2843432	291	pir.E70552	Mycobacterium tuberculosis H37Rv Rv3592	48.5	69.1	97	hypothetical protein
2941	6441	2845139	2845558	420	GSP:Y29188	Pseudomonas aeruginosa ORF24222	57.0	63.0	66	virulence factor
2942	6442	6442 2845889	2846101	213	GSP_Y29193	Pseudomonas aeruginosa ORF25110	54.0	55 0	72	virulence factor

5
10
15
20
25
30
35
40
45
50

	Function	virulence factor	CIpC adenosine triphosphatase / ATP-binding proteinase	inosine monophosphate dehydrogenase	transcription factor	phenol 2-manooxygenase					lincomycin resistance protein lincomycin resistance protein	hypothetical protein	lysyl-tRNA synthetase	pantoatebeta-alanine ligase			hypothetical membrane protein	2-amino-4-hydroxy-6- hydroxymethyldihydropteridine pyrophosphokinase	dihydroneopterin aldolase	dihydropleroate synthase
	Matched length (a.a.)	55	832	469	316	089				ļ	481	240	511	268			138	158	118	268
	Similarity (%)	75.0	86.2	70.2	62.7	6.09					100.0	55.8	71.2	52.6			9.69	0.69	69.5	75.0
	Identity (%)	74.0	58.5	37.1	24.7	33.5					100.0	26.7	41.7	29.9			29.0	42.4	38.1	51.5
Table 1 (continued)	Homologous gene	Pseudomonas aeruginosa ORF25110	Bacillus subtilis 168 mecB	Bacillus cereus ts-4 impdh	Rhodococcus rhodochrous nitR	Trichosporon cutaneum ATCC 46490					Corynebacterium glutamicum Corynebacterium glutamicum ImrB	Mycobacterium tuberculosis H37Rv Rv3517	Bacillus stearothermophilus lysS	Corynebacterium glutamicum ATCC 13032 panC			Mycobacterium leprae MLCB2548.04c	Methylobacterium extorquens AM1 folK	Bacillus subtilis 168 folB	Mycobacterium leprae folP
	db Match	GSP:Y29193	sp.MECB_BACSU	gp:AB035643_1	pir.JC6117	sp:PH2M_TRICU					gp:AF237667_1	pir.G70807	gp.AB012100_1	gp.CGPAN_2			gp:MLCB2548_4	sp.HPPK_METEX	sp.FOLB_BACSU	gp: AB028656_1
	ORF (bp)	321	2775	1431	1011	1785	1716	1941	1722	162	1443	951	1578	798	693	798	465	477	390	837
	Terminal (nt)	2846506	2844166	2848659	2849779	2851815	2853732	2855709	2857516	2859205	2857613	2859195	2860505	2862132	2862929	2863624	2864384	2864867	2865346	2865731
	Initial (nt)	2846186	2846940	2847229	2848769	2850031	6448 2852017	2853769	2855795	2859044	2859055	2860145	2862082	2862929	2863621	2864421	2864848	2865343	2865735	
	SEO NO.	6443	6444	6445	6446	6447	6448	6449	6450	6451	6452	6453	6454	6455	6456	6457	6458	6459	6460	6461

	Function	GTP cyclohydrolase I		cell division protein FtsH	hypoxanthine phosphoribosyltransferase	cell cycle protein MesJ or cytosine deaminase-related protein	D-alanyl-D-alanine carboxypeptidase	inorganic pyrophosphatase		spermidine synthase	hypothetical membrane protein hypothetical membrane protein	hypothetical protein	hypothetical protein	hypothetical protein	PTS system, beta-glucosides- permease II ABC component		ferredoxin reductase	hypothetical protein	bacterial regulatory protein, marR family
	Matched length (a.a.)	188		782	165	310	459	159		205	132	144	173	202	68		411	97	135
	Similarity (%)	86.2		0.69	83.0	8.99	51.4	73.6		80.7	885.4 44.	63.2	60.1	72.3	59.6		9 69	73.2	593
	Identity (%)	9.09		999	51.5	41.0	27.2	49.7		56.0	38.8	36.8	36.4	44.6	30.3		38.0	46.4	26.7
Table 1 (continued)	Homologous gene	Bacillus subtilis 168 mtrA			Salmonella typhimurium GP660 hprt	Mycobacterium tuberculosis H37Rv Rv3625c	Actinomadura sp. R39 dac	Escherichia coli K12 ppa		Mycobacterium tuberculosis H37Rv speE	Mycobacterium tuberculosis	Mycobacterium tuberculosis H37Rv Rv2599	Mycobacterium tuberculosis H37Rv Rv2598	Mycobacterium tuberculosis H37Rv Rv2597	Bacillus subtilis 168 bgIP		Nocardioides sp. KP7 phdD	Streptomyces coelicolor A3(2) SCH69.09c	Burkholderia pseudomallei ORF E
	db Match	sp.GCH1_BACSU			gp.AF008931_1	sp.YZC5_MYCTU	sp.DAC_ACTSP	sp:IPYR_ECOLI		pir:H70886	sp:Y0B1_MYCTU	sp:Y0B2_MYCTU	sp:Y0B3_MYCTU	sp.Y084_MYCTU	sp PTBA_BACSU		gp:AB017795_2	9p:SCH69_9	prf 2516298U
	ORF (bp)	588	915	2580	582	1691	1233	474	219	1539	399	411	498	609	249	264	1233	288	444
	Terminal (nt)	2866586	2868385	2867169	2869863	2870499	2871445	2873399	2873393	2873905	2875434	2875870	2876280	2876777	2877455	2877595	2878478	2880252	2880987
	Initial (nt)	2867173	2867471	2869748		2871389	2872677	2872926	2873611		2875832	2876280	2876777	2877385	2877703	2877858	2879710	2879965	6479 2880544
	SEQ NO	6462	6463		6465	6466	6467	6468	6469	6470	6471	6472	6473	6474	6475	6476		6478	
	SEQ		-			2966	2967	2968	2969	1	2971	2972	2973	2974	2975	2976	2977	2978	2979

5	•
10	
15	
20	
25	
30	
35	
40	
45	
5 <i>ọ</i>	

	Function	peptide synthase		phenylacetaldehyde dehydrogenase	hypothetical protein	hypothetical protein	hypothetical protein	heat shock protein or chaperon or groEL protein						The state of the s		hypothetical protein			peptidase			Na+/H+ antiporter or multiple resistance and pH regulation related protein A or NADH dehydrogenase
	Matched length (a.a.)	1241		488	241	54	31	548								1236			447			797
	Similarity (%)	51.6		63.7	79.7	63.0	80.0	100.0			7.7			X)		42.3			0.89			683
	Identity (%)	28.4		35.0	57.3	62.0	74.0	99.5								21.7			37.1			35.6
Table 1 (continued)	Homologous gene	Streptomyces roseosporus cpsB		Escherichia coli K12 padA	Campylobacter jejuni Cj0604	Mycobacterium tuberculosis	Mycobacterium tuberculosis	Brevibacterium flavum MJ-233								Homo sapiens MUC5B			Mycobacterium tuberculosis H37Rv Rv2522c			Staphylococcus aureus mnhA
	db Match	prf 2413335A		prf.2310295A	gp.CJ11168X2_25	GP.MSGTCWPA_1	GP_MSGTCWPA_1	gsp.R94368								prf.2309326A			pir.G70870			prf.2504285B
	ORF (bp)	3885	1461	1563	918	162	177	1644	180	1209	963	1986	2454	27.07	66/7	3591	2775	612	1371	579	009	3057
	Terminal (nt)	2884882	2881844	2884935	2886916	2890346	2890553	2888897	2890751	2890930	2892138	2893100	2005072	3,0000	979/697	2900330	2903964	2906639	2908885	2909788	2909231	2913228
	Initial (nt)	2880998	2883304	2886497	2887833	2890185	2890377	2890540	2890930	2892138	2893100	2895085	3037000			2903920	2906738	2907250	2907515	2909210	2909830	2910172
	SEQ NO.	6480	6481	6482	6483	6484	6485	6486	6487	6488	6489	6490	6404	640	6492	6493	6494	6495	6496	6497	6498	6499
	SEQ NO (DNA)	2980	2981	2982	2983	2984	2985	2986	2987	2988	2989	2990	1000	1867	2992	2993	2994	2995	2996	2997	2998	2999

5	
10	
15	
20	
25	
30	
35	
40	
45	
50	

,																
	Function	Na+/H+ antiporter or multiple resistance and pH regulation related protein C or cation transport system protein	Na+/H+ antiporter or multiple resistance and pH regulation related protein D	Na+/H+ antiporter or multiple resistance and pH regulation related protein E	K+ efflux system or multiple resistance and pH regulation related protein F	Na+/H+ antiporter or multiple resistance and pH regulation related	hypothetical protein	hypothetical protein		polypeptide deformylase	hypothetical protein	acetyltransferase (GNAT) family or N terminal acetylating enzyme			exodeoxyribonuclease III or exonuclease	cardiolipin synthase
	Matched length (a.a.)	104	523	161	7.1	121	178	334		184	7.1	339			31	513
,	Similarity (%)	81.7	72.1	6.09	66.2	63.6	54.5	61.7		6.09	70.4	54.2			59.9	62.0
	Identity (%)	44.2	35.2	26.7	32.5	25.6	24.7	27.0		37.5	47.9	31.3			30.8	27.9
Table 1 (continued)	Homologous gene	Bacillus firmus OF4 mrpC	Bacillus firmus OF4 mrpD	Bacillus firmus OF4 mrpE	Rhizobium meliloti phaF	Staphylococcus aureus mnhG	Mycobacterium tuberculosis H37Rv lipV	Escherichia coli K12 ybdK		Bacillus subtilis 168 def	Mycobacterium tuberculosis H37Rv Rv0430	Mycobacterium tuberculosis H37Rv Rv0428c			Salmonella typhimurium LT2 xthA	Bacillus firmus OF4 cls
	db Match	gp <sup>.</sup> AF097740_3	gp:AF097740_4	gp.AF097740_5	prf.2416476G	prf.2504285H	pir:D70594	sp:YBDK_ECOLI		sp:DEF_BACSU	pir:D70631	pir:870631			gp:AF108767_1	gp:BFU88888_2
	ORF (bp)	489	1668	441	273	378	594	1128	663	579	252	1005	699	630	789	1500
	Terminal (nt)	2913723	2915416	2915922	2916201	2916582	2917024	2917630	2918819	2920293	2919490	2921290	2919808	2920220	2922108	2923617
	Initial (nt)	2913235	2913749	2915482	2915929	2916205	2917617	2918757	2919481	2919715	2919741	2920286	2920476	2920849	2921320	2922118
	SEQ NO.	6500	6501	6502	6503	6504	6505	9059	6507	6508	6209	6510	6511	6512	6513	6514
	SEQ NO. (DNA)	3000	3001	3002	3003	3004	3005	3006	3007	3008	3009	3010	3011	3012	3013	3014
						-										

5	
10	
15	
20	
25	•
30	
35	
40	
45	
50	

1	$\neg$		T	Ī	i		ا ت	- 1		1		ī					ī		
Function		membrane transport protein or bicyclomycin resistance protein	sodium dependent phosphate pump	phenazine biosynthesis protein		ABC transporter	ABC transporter ATP-binding proteir	mutator mutT protein	hypothetical membrane protein	glutamine-binding protein precursor	serineAhreonine kinase		ferredoxin/ferredoxin-NADP reductase	acetyltransferase (GNAT) family				phosphoribosylglycinamide formyltransferase	
Matched length (a a)		393	382	289		255	309	168	423	270	805		457	156				379	
Similarity (%)		67.2	68.9	56.4		8.09	66.3	68.5	70.2	64.8	63.5		67.8	60.3				82.6	
Identity (%)		31.6	28.5	. 38.8		24.3	36.9	47.6	35.0	31.5	41.2		37.2	34.0				59.1	
Homologous gene		Escherichia coli K12 bcr	Vibrio cholerae JS1569 nptA	Pseudomonas aureofaciens 30- 84 phzC		Streptomyces coelicolor A3(2) SCE8.16c	Bacillus licheniformis ATCC 9945A bcrA	Mycobacterium tuberculosis H37Rv Rv0413	Mycobacterium tuberculosis	Bacillus stearothermophilus NUB36 glnH	Mycobacterium tuberculosis H37Rv Rv0410c pknG		Bos taurus.	Escherichia coli K12 elaA			*	Bacillus subtilis 168 purT	
db Match		sp.BCR_ECOLI	gp.VCAJ10968_1	sp.PH2C_PSEAR		gp:SCE8_16	sp.BCRA_BACLI	pir.C70629	pir:870629 pir:870629	SP. GLNH_BACST	pir.H70628		sp. ADRO_BOVIN	sp:ELAA_ECOLI				sp:PURT_BACSU	
ORF (bp)	654	1194	1164	840	633	768	936	501	1386 386 386	1032	2253	747	1365	546	1062	1029	399	1194	888
Terminal (nt)	2924844	2923954	2926704	2926707	2927651	2927551	2928302	2929256	2931338	2932371	2934829	2932652	2939767	2940452	2940447	2941472	2942609	2943012	2945639
Initial (nt)	2924191	2925147	2925541	2927546	2928283	2928318	2929237	2929756	2929951	2931340	2932577	2933398	2938403	2939907	2941508	2942500	2943007	2944205	2946526
SEO NO (a.a.)	6515						6521	6522	6523	6524			6527	+	6259	6530	6531		6533
SEQ NO (DNA)	3015	3016	3017	3018	3019	3020	3021	3022	3823	3024	3025	3026	3027	3028	3029	3030	3031	3032	3033
	SEQ Initial Terminal ORF db Match Homologous gene (%) (nt) (bp) (bp)	SEQ Initial NO.         Initial (nt)         Terminal (nt)         ORF (bp)         db Match         Homologous gene (%)         Identity (%)         Similarity (a a.)         Matched (ea.)           63.15         2924191         2924844         654	SEQ NO. (a.a.)         Initial (nt)         Terminal (nt)         ORF (pp)         db Match (bp)         Matched (bp)         Homologous gene (a.a.)         Identity (%)         Similarity (%)         Matched (%)         M	SEQ (nt)         Initial (nt)         Terminal (nt)         QRF (bp)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)           (a.a.)         (nt)         (nt)         (nt)         (hp)         <	SEQ Initial Note (a.a.)         Terminal (nt)         ORF (nt)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Ma	SEQ Initial NO.         Terminal (nt) (nt)         QRF (pp)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Match	SEQ (nt) (nt) (nt) (nt) (bp)         Terminal (bp)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)	SEQ Initial Note (it)         Terminal (it)         ORF (it)         db Match         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matc	SEQ Initial NO. (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt)	SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity (%)         Similarity (%)         Matched (%)           NO (n1)         (n1)         (n1)         (nt)         (nt)         (nt)         (ph)         (ph) <t< td=""><td>SEQ NO. Initial         Initial (III)         Terminal (III)         ORF (bb)         db Match (bb)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Ma</td><td>SED         Initial         Terminal         ORF         db Match         Homologous gene         Identity (%)         Similarity length (%)         Matched (%)         Matc</td><td>SEQ NO.         Initial (Int)         Terminal (Int)         ORF (Int)         db Match (Int)         Homologous gene (Identity)         Identity (Identity)         Similarity (Identity)         Matched (Identity)           65.15 5.2924191         2924844 2925147         654 2925147         2923844 2925547         654 2925147         2926670 2925341         1164 2925541         1194 2925541         1194 2925541         1194 2925541         40 km cholerae JS 1569 nptA 2925541         28.5 292 292 292 292 292 292 292 292 292 29</td><td>SEO         Initial         Terminal         ORF         db Malch         Homologous gene         Identity (%)         Similarity length (%)         Amulached (%)         Amul</td><td>SEQ         Initial         Terminal         ORF         date Match         Homologous gene         (%)         Similaring (%)         Matched (%)           NO         (III)         (III)         (ID)         (ID)<td>SEQ         Initial         Terminal (PM)         ORF (Match         Abatch         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)           NO         (Ini)         (Ini)         (In)         (PM)         Ab Match         Homologous gene (%)         <td< td=""><td>SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity         Similarity (%)         Matched (%)<td>SEQ         Initial         Terminal         ORF         db Malch         Homologous gene         Identity         Similariarity         Matched (%)         Matched (%)</td><td>SEO         Initial (nt)         (Int)         (Int)</td></td></td<></td></td></t<>	SEQ NO. Initial         Initial (III)         Terminal (III)         ORF (bb)         db Match (bb)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Ma	SED         Initial         Terminal         ORF         db Match         Homologous gene         Identity (%)         Similarity length (%)         Matched (%)         Matc	SEQ NO.         Initial (Int)         Terminal (Int)         ORF (Int)         db Match (Int)         Homologous gene (Identity)         Identity (Identity)         Similarity (Identity)         Matched (Identity)           65.15 5.2924191         2924844 2925147         654 2925147         2923844 2925547         654 2925147         2926670 2925341         1164 2925541         1194 2925541         1194 2925541         1194 2925541         40 km cholerae JS 1569 nptA 2925541         28.5 292 292 292 292 292 292 292 292 292 29	SEO         Initial         Terminal         ORF         db Malch         Homologous gene         Identity (%)         Similarity length (%)         Amulached (%)         Amul	SEQ         Initial         Terminal         ORF         date Match         Homologous gene         (%)         Similaring (%)         Matched (%)           NO         (III)         (III)         (ID)         (ID) <td>SEQ         Initial         Terminal (PM)         ORF (Match         Abatch         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)           NO         (Ini)         (Ini)         (In)         (PM)         Ab Match         Homologous gene (%)         <td< td=""><td>SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity         Similarity (%)         Matched (%)<td>SEQ         Initial         Terminal         ORF         db Malch         Homologous gene         Identity         Similariarity         Matched (%)         Matched (%)</td><td>SEO         Initial (nt)         (Int)         (Int)</td></td></td<></td>	SEQ         Initial         Terminal (PM)         ORF (Match         Abatch         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)           NO         (Ini)         (Ini)         (In)         (PM)         Ab Match         Homologous gene (%)         (%) <td< td=""><td>SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity         Similarity (%)         Matched (%)<td>SEQ         Initial         Terminal         ORF         db Malch         Homologous gene         Identity         Similariarity         Matched (%)         Matched (%)</td><td>SEO         Initial (nt)         (Int)         (Int)</td></td></td<>	SEQ         Initial         Terminal         ORF         db Match         Homologous gene         Identity         Similarity (%)         Matched (%) <td>SEQ         Initial         Terminal         ORF         db Malch         Homologous gene         Identity         Similariarity         Matched (%)         Matched (%)</td> <td>SEO         Initial (nt)         (Int)         (Int)</td>	SEQ         Initial         Terminal         ORF         db Malch         Homologous gene         Identity         Similariarity         Matched (%)         Matched (%)	SEO         Initial (nt)         (Int)         (Int)

	Function	insertion element (IS3 related)	insertion element (IS3 related)	two-component system sensor histidine kinase	transcriptional regulator		adenylosuccinate synthetase.	hypothetical protein		hypothetical membrane protein	fructose-bisphosphate aldolase	hypothetical protein	methyltransferase	orotate phosphoribosyltransferase	hypothetical protein	3-mercaptopyrwate sulfurtransferase			
	Matched length (a.a.)	295	89	349	218		427 a	204		359	344	304	182	174	250	294			
	Similarity (%)	6.06	84.3	51.3	65.6		95.3	59.3		100.0	100.0	100.0	91.2	65.5	0.09	56.1			
	Identity (%)	97.7	67.4	22.4	31.7		89.7	34.3		100.0	99.7	100.0	6.97	39.1	27.6	29.6			
Table 1 (continued)	Homologous gene	Corynebacterium glutamicum orf2	Corynebacterium glutamicum orf1	Streptomyces thermoviolaceus opc-520 chiS	Bacillus brevis ALK36 degU		Corynebacterium ammoniagenes purA	Mycobacterium tuberculosis H37Rv Rv0358		Corynebacterium glutamicum	Corynebacterium glutamicum AS019 ATCC 13059 fda	Corynebacterium glutamicum AS019 ATCC 13059 ORF1	Mycobacterium tuberculosis H37Rv Rv0380c	Pyrococcus abyssi pyrE	Mycobacterium tuberculosis H37Rv Rv0383c	Homo sapiens mpsT			
	db Match	pir S60890	pir S60889	gp:AB016841_1	sp.DEGU_BACBR		gp.AB003160_1	pir.G70575		Sp: YFDA CORGL	pir.S09283	gp:CGFDA_1	pir.G70833	gp:AF058713_1	pir:870834	sp.THTM_HUMAN			
	ORF (bp)	894	267	1140	618	225	1290	759	264	1167	1032	951	618	552	972	852	720	279	399
	Terminal (nt)	2946698	2947620	2948049	2949265	2950431	2950434	2952691	2952972	2952975	2954241	2955523	2956830	2957485	2958139	2959520	2960468	2962730	2963198
	Initial (nt)	2947591	2947886	2949188	2949882	2950207	2951723	2951933	2952709	2854141	2955272	2956473	2957447	2958036	2959110	2960371	6549 2961187	2963008	3051 6551 2963596
	SEQ NO	6534	6535	6536	6537	6538	6239	6540	6541	6542	6543	6544	6545	6546	6547	6548	6549	3050 6550	6551
	SEQ NO.	3034	3035	3036	3037		3039	3040	3041	3042	3043	3044	3045	3046	3047	3048	3049	3050	3051

10	
15	
20	
25	
30	
35	
40	
45	

a
ĕ
2
듣
ĕ
೭
_
풀
逦

									- 1							
Function	virulence factor	virulence factor	virulence factor	sodium/glutamate symport carrier protein	cadmium resistance protein	cation efflux system protein (zinc/cadmium)	monooxygenase or oxidoreductase or steroid monooxygenase	alkanal monooxygenase alpha chain		cystathionine gamma-lyase	bacterial regulatory protein, faci family	rifampin ADP-ribosyl transferase	ııfampin ADP-ribosyl transferase	hypothetical protein	hypothetical protein	oxidoreductase
Matched length (a a )	59	200	132	489	108	283	476	399		375	184	68	99	361	204	386
Similarity (%)	82.0	55.0	63.0	54.8	71.3	63.3	45.4	47.4		62.4	67.9	65.2	87.5	56.2	64.7	9.09
Identity (%)	76.0	38.0	62.0	24.7	37.0	23.7	22.5	21.1		36.5	40.2	49.4	73.2	30.5	33.8	31.9
Homologous gene	Pseudomonas aeruginosa ORF24222	Pseudomonas aeruginosa ORF23228	Pseudomonas aeruginosa ORF25110	Synechocystis sp. PCC6803 str0625	Staphylococcus aureus cadC	Pyrococcus abyssi Orsay PAB0462	Rhodococcus rhodochrous IFO3338	Kryptophanaron alfredi symbiont luxA iuxA		Escherichia coli K12 metB	Streptomyces coelicolor A3(2) SC1A2.11	Streptomyces coelicolor A3(2) SCE20.34c arr	Streptomyces coelicolor A3(2) SCE20.34c arr	Mycobacterium tuberculosis H37Rv Rv0837c	Mycobacterium tuberculosis H37Rv Rv0836c	Mycobacterium Iuberculosis H37Rv Rv0385
db Match	GSP Y29188	GSP: Y29182	GSP: Y29193	pir:S76683	sp:CADF_STAAU	pir.H75109	gp:AB010439_1	sp.LUXA_KRYAS		Sp.METB_ECOLI	gp:SC1A2_11	gp:SCE20_34	gp:SCE20_34	pir:E70812	pir:D70812	pir.D70834
ORF (bp)	177	762	396	1347	387	828	1170	1041	762	1146	267	240	183	1125	732	1179
Terminal (nt)	2964434	2965837	2965583	2966458	2968789	2969808	2971003	2972057	2971338	2972060	2973230	2974200	2974382	2975591	2976360	2977774
Initial (nt)	2964258	2965076	2965188	2967804	2968403	2968951	2969834	2971017	2972099	2973205	2973796	2973961	2974200	2974467	2975629	2976596
SEQ NO.	6552	6553	6554	6555	6556	6557	6558	6229	6560	6561	6562	6563	6564	6565	9959	6567
SEQ NO.	3052	3053	3054	3055	3056	3057	3058	3059	3060	3061	3062	3063	3064	3065	3066	3067
	SEQ Initial Terminal ORF db Match Homologous gene (%) (nt) (bp) (bp)	SEQ Initial (a.a.)         Initial (ht)         Terminal (ht)         QRF (ht)         db Match         Homologous gene (%)         Homologous gene (%)         Identity (%)         Matched (%)         Matched (%)         Homologous gene (%)         Image: (%)	SEQ Initial (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt)	SEQ (nt) (nt) (nt) (nt) (hp)         Terminal (hp) (hp)         About (hp) (hp) (hp)         Homologous gene (hp) (hp) (hp) (hp)         Homologous gene (hp) (hp) (hp) (hp) (hp) (hp) (hp) (hp)	SEQ (nt)         Initial (nt)         Terminal (nt)         ORF (nt)         db Match (pp)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matched (%)	SEQ NO. (nt)         Initial (nt)         Terminal (nt)         ORF (pp)         db Match (pp)         Homologous gene (pp)         Identity (pp)         Similarity (pp)         Matched (pp)           6552         2964258         2964434         177         GSP-Y29188         Pseudomonas aeruginosa ORF23228         76.0         82.0         59           6553         2965076         2965837         76.2         GSP-Y29182         Pseudomonas aeruginosa ORF2328         38.0         55.0         200           6554         2965188         2965583         396         GSP-Y29193         Pseudomonas aeruginosa ORF25110         62.0         63.0         132           6555         2967804         2966458         1347         pir.S78683         Synechocystis sp. PCC6803 str0625         24.7         54.8         489           6556         2968403         2968789         387         sp.CADF_STAAU         Staphylococcus aureus cadC         37.0         71.3         108	SEQ NO. (a.a.)         Initial (nt)         Terminal (nt)         ORF (bp)         db Match         Homologous gene         Identity (%)         Similarity (%)         Matched (%)         Matched (%) <td>SEQ Initial NOT (nt)         Terminal (nt)         ORF (pp)         db Match         Homologous gene (pp)         Identity (pp)         Similarity (pp)         Matched (pp)</td> <td>SEQ (nt) (nt)         Initial (bp) (lp)         db Match (bp) (lp)         Homologous gene (lp)         Identity (lp) (lp)         Similarity (la a) (lp)         Matched (la a) (lp)           NO (nt) (nt) (lp) (lp)         (nt) (lp) (lp)         (lp) (lp) (lp)         Pseudomonas aeruginosa         76.0         82.0         59           6552 (lp) (lp) (lp) (lp) (lp) (lp)         2965016         2965837         762 (lp) (lp) (lp) (lp) (lp) (lp) (lp) (lp)</td> <td>SEQ NO.         Initial (nt)         Terminal (nt)         ORF (b)         db Match (b)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matched (%)<td>SEC (nitial)         Initial (nt)         Terminal (nt)         ORF (nt)         Homologous gene (ms)         Identity (ms)         Similarity (matched)         Matched (ms)           NO. (nt)         (nt)<td>SEC NO NO SESS2         Initial (nt)         Terminal (nt)         ORF (nt)         db Match (nt)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matc</td><td>SEC NO Initial         Initial (Ini)         Terminal (Ini)         ORF (Ini)         db Match (Ini)         Homologous gene (Ini)         Homologous gene (Ini)         Identity (Ini)         Similarity (Ini)         Matched (Ini)         Matched (Ini)</td><td>SEC NO Initial         Initial (In)         Terminal (In)         ORF (In)         Terminal (In)         ORF (In)         Homologous gene (In)         Identity (In)         Similarity (In)         Matched (In)           6552         2964256         2964434         177         GSP-Y29188         Pseudomonas aeruginosa ORF24222         76.0         82.0         59           6553         2965076         2965837         76.2         GSP-Y29182         Pseudomonas aeruginosa ORF23108         38.0         55.0         200           6554         2965188         2965863         386         GSP-Y29193         Pseudomonas aeruginosa ORF23100         38.0         55.0         200           6555         2966403         2965869         1347         pir.S76683         Spredocystls sp. PCC6803         24.7         54.8         489           6556         2968403         2968789         387         sp.CADF_STAAU         Slaphylococcus aureus cadC         37.0         71.3         108           6556         2968403         1170         gp. AB010439-1         Fhotococcus abyssi Orsay         23.7         63.3         28.3           6556         2972097         1141         sp. LUXA, KRYAS         Kryptophanaron alifedi symbiont         21.1         47.4         399</td><td>SEC NO         Initial (III)         Terminal (IVI)         ORF (PA)         Homologous gene (PA)         Identity (PA)         Matched (PA)         Matched (PA</td><td>SEG         Initial         Terminal (mt)         ORF         db Match         Homologous gene         Identity (%)         Matched (</td></td></td>	SEQ Initial NOT (nt)         Terminal (nt)         ORF (pp)         db Match         Homologous gene (pp)         Identity (pp)         Similarity (pp)         Matched (pp)	SEQ (nt) (nt)         Initial (bp) (lp)         db Match (bp) (lp)         Homologous gene (lp)         Identity (lp) (lp)         Similarity (la a) (lp)         Matched (la a) (lp)           NO (nt) (nt) (lp) (lp)         (nt) (lp) (lp)         (lp) (lp) (lp)         Pseudomonas aeruginosa         76.0         82.0         59           6552 (lp) (lp) (lp) (lp) (lp) (lp)         2965016         2965837         762 (lp) (lp) (lp) (lp) (lp) (lp) (lp) (lp)	SEQ NO.         Initial (nt)         Terminal (nt)         ORF (b)         db Match (b)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matched (%) <td>SEC (nitial)         Initial (nt)         Terminal (nt)         ORF (nt)         Homologous gene (ms)         Identity (ms)         Similarity (matched)         Matched (ms)           NO. (nt)         (nt)<td>SEC NO NO SESS2         Initial (nt)         Terminal (nt)         ORF (nt)         db Match (nt)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matc</td><td>SEC NO Initial         Initial (Ini)         Terminal (Ini)         ORF (Ini)         db Match (Ini)         Homologous gene (Ini)         Homologous gene (Ini)         Identity (Ini)         Similarity (Ini)         Matched (Ini)         Matched (Ini)</td><td>SEC NO Initial         Initial (In)         Terminal (In)         ORF (In)         Terminal (In)         ORF (In)         Homologous gene (In)         Identity (In)         Similarity (In)         Matched (In)           6552         2964256         2964434         177         GSP-Y29188         Pseudomonas aeruginosa ORF24222         76.0         82.0         59           6553         2965076         2965837         76.2         GSP-Y29182         Pseudomonas aeruginosa ORF23108         38.0         55.0         200           6554         2965188         2965863         386         GSP-Y29193         Pseudomonas aeruginosa ORF23100         38.0         55.0         200           6555         2966403         2965869         1347         pir.S76683         Spredocystls sp. PCC6803         24.7         54.8         489           6556         2968403         2968789         387         sp.CADF_STAAU         Slaphylococcus aureus cadC         37.0         71.3         108           6556         2968403         1170         gp. AB010439-1         Fhotococcus abyssi Orsay         23.7         63.3         28.3           6556         2972097         1141         sp. LUXA, KRYAS         Kryptophanaron alifedi symbiont         21.1         47.4         399</td><td>SEC NO         Initial (III)         Terminal (IVI)         ORF (PA)         Homologous gene (PA)         Identity (PA)         Matched (PA)         Matched (PA</td><td>SEG         Initial         Terminal (mt)         ORF         db Match         Homologous gene         Identity (%)         Matched (</td></td>	SEC (nitial)         Initial (nt)         Terminal (nt)         ORF (nt)         Homologous gene (ms)         Identity (ms)         Similarity (matched)         Matched (ms)           NO. (nt)         (nt) <td>SEC NO NO SESS2         Initial (nt)         Terminal (nt)         ORF (nt)         db Match (nt)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matc</td> <td>SEC NO Initial         Initial (Ini)         Terminal (Ini)         ORF (Ini)         db Match (Ini)         Homologous gene (Ini)         Homologous gene (Ini)         Identity (Ini)         Similarity (Ini)         Matched (Ini)         Matched (Ini)</td> <td>SEC NO Initial         Initial (In)         Terminal (In)         ORF (In)         Terminal (In)         ORF (In)         Homologous gene (In)         Identity (In)         Similarity (In)         Matched (In)           6552         2964256         2964434         177         GSP-Y29188         Pseudomonas aeruginosa ORF24222         76.0         82.0         59           6553         2965076         2965837         76.2         GSP-Y29182         Pseudomonas aeruginosa ORF23108         38.0         55.0         200           6554         2965188         2965863         386         GSP-Y29193         Pseudomonas aeruginosa ORF23100         38.0         55.0         200           6555         2966403         2965869         1347         pir.S76683         Spredocystls sp. PCC6803         24.7         54.8         489           6556         2968403         2968789         387         sp.CADF_STAAU         Slaphylococcus aureus cadC         37.0         71.3         108           6556         2968403         1170         gp. AB010439-1         Fhotococcus abyssi Orsay         23.7         63.3         28.3           6556         2972097         1141         sp. LUXA, KRYAS         Kryptophanaron alifedi symbiont         21.1         47.4         399</td> <td>SEC NO         Initial (III)         Terminal (IVI)         ORF (PA)         Homologous gene (PA)         Identity (PA)         Matched (PA)         Matched (PA</td> <td>SEG         Initial         Terminal (mt)         ORF         db Match         Homologous gene         Identity (%)         Matched (</td>	SEC NO NO SESS2         Initial (nt)         Terminal (nt)         ORF (nt)         db Match (nt)         Homologous gene (%)         Identity (%)         Similarity (%)         Matched (%)         Matc	SEC NO Initial         Initial (Ini)         Terminal (Ini)         ORF (Ini)         db Match (Ini)         Homologous gene (Ini)         Homologous gene (Ini)         Identity (Ini)         Similarity (Ini)         Matched (Ini)         Matched (Ini)	SEC NO Initial         Initial (In)         Terminal (In)         ORF (In)         Terminal (In)         ORF (In)         Homologous gene (In)         Identity (In)         Similarity (In)         Matched (In)           6552         2964256         2964434         177         GSP-Y29188         Pseudomonas aeruginosa ORF24222         76.0         82.0         59           6553         2965076         2965837         76.2         GSP-Y29182         Pseudomonas aeruginosa ORF23108         38.0         55.0         200           6554         2965188         2965863         386         GSP-Y29193         Pseudomonas aeruginosa ORF23100         38.0         55.0         200           6555         2966403         2965869         1347         pir.S76683         Spredocystls sp. PCC6803         24.7         54.8         489           6556         2968403         2968789         387         sp.CADF_STAAU         Slaphylococcus aureus cadC         37.0         71.3         108           6556         2968403         1170         gp. AB010439-1         Fhotococcus abyssi Orsay         23.7         63.3         28.3           6556         2972097         1141         sp. LUXA, KRYAS         Kryptophanaron alifedi symbiont         21.1         47.4         399	SEC NO         Initial (III)         Terminal (IVI)         ORF (PA)         Homologous gene (PA)         Identity (PA)         Matched (PA)         Matched (PA	SEG         Initial         Terminal (mt)         ORF         db Match         Homologous gene         Identity (%)         Matched (

•		
	5	
	10	
	15	
	20	
	25	
	30	
	25	
	35	
	40	
	45	
	50	

						Table 1 (continued)				
SEQ	SEQ NO	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched length (a.a.)	Function
3068		2978644	2977847	798	pir. B69109	Methanobacterium thermoautotrophicum Delta H MTH1811	32.0	67.3	275	N-carbamoyl-D-amino acid amidohydrolase
3069	6969	2978737	2978979	243						
3070		2978982		1134	gp.SC4A7_3	Streptomyces coelicolor A3(2) SC4A7.03	28.0	55.4	289	hypothetical protein
3071	6571	2980887	2981216	330	GP. ABCARRA_2	Azospirillum brasilense carR	38.0	44.0	108	novel two-component regulatory system
3072	6572	2981698	2980181	1518	prf.2104333D	Rhodococcus erythropolis thcA	9.69	90.3	507	aldehyde dehydrogenase
3073			2982023	438	gp.SAU43299_2	Streptomyces albus G hspR	47.4	70.4	135	heat shock transcription regulator
3074	6574	2983679		1185		Mycobacterium tuberculosis H37Rv RV0352 dnaJ	26.7	80.1	397	heat shock protein dnaJ
3075	6575	2984522	2983887	929	sp.GRPE_STRCO	Streptomyces coelicolor grpE	38.7	66.5	212	nucleotide exchange factor grpE protein bound to the ATPase domain of the molecular chaperone DnaK
3076	6576	2986397	2984544	1854	gsp:R94587	Brevibacterium flavum MJ-233 dnaK	9.66	96 8	618	heat shock protein dnaK
. 3077	6577	2986833	2988164	1332	gp.SCF6_8	Streptomyces coelicolor A3(2) SCF6.09	42.6	79.0	338	hypothetical membrane protein
3078	6578	2988846	2988214	633	sp.PFS_HELPY	Helicobacter pylori HP0089 mtn	27.2	0 09	195	5'-methylthioadenosine nucleosidase and S- adenosylhomocysteine nucleosidase
3079	6259	2990045	2988846	1200						
3080	0859	2991718	2992602	885						
3081	6581	2993286	2989954	3333	sp.CUT3_SCHPO	Schizosaccharomyces pombe cut3	18.9	48.4	1311	chromosome segregation protein
3082	2 6582	2993921	2993286	636						
3083	3 6583	2995405	2993921	1485						
3084	4 6584	2996781	2995747	1035	1035 sp ADH2_BACST	Bacillus stearothermophilus DSM 2334 adh	20.0	81.7	334	atcohol dehydrogenase
!										

10	Function					hypothetical membrane protein	hypothetical protein		sulfate adenylyltransferase, subunit 1	sulfate adenylyltransferase small chain	phosphoadenosine phosphosulfate	ferredoxinnitrate reductase	ferredoxin/ferredoxin-NADP reductase	huntingtin interactor			alkylphosphonate uptake protein and C-P lyase activity	hypothetical protein	ammonia monooxygenase		
15	Matched length (a.a.)					301	252		414	308	212	502	487	144			142	80	161		
20	Similarity (%)					70.1	53.2		78.3	70.1	64.2	65.5	61.4	59.7			6.65	66.3	76.4		
	Identity (%)					43.5	32.5		47.3	46.1	39.2	34.5	30.8	32.6			26.8	20.0	39.1		
25 (pa							(3(5)					7942	ə				3	13(2)	MZ ID		
56 September 25 Se	Homologous gene					Bacillus subtilis ytnM	Streptomyces coelicolor A3(2) SC7A8.10c		Escherichia coli K12 cysN	Escherichia coli K12 cysD	Bacillus subtilis cysH Bacillus subtilis cysH	Synechococcus sp. PCC 7942	Saccharomyces cerevisiae FL200 arh1	Homo sapiens hypE			Escherichia coli K12 phnB	Streptomyces coelicolor A3(2) SCE68.10	Pseudomonas putida DSMZ ID 88-260 amoA		
40	db Match					pir:F69997	gp:SC7A8_10		sp.CYSN_ECOLI	sp.cysD_Ecoul	sp.CYH1_BACSU	sp.NIR_SYNP7	sp:ADRO_YEAST	prf:2420294J			sp:PHNB_ECOL!	gp:SCE68_10	gp.PPAMOA_1		
	ORF (bp)	216	207	189	261	927	723	915	1299	912	669	1683	1371	1083	237	534	414	366	522	321	486
45	Terminal (nt)	2997366	2997481	2997876	2997963	2998528	2999478	3002426	3000241	3001542	3882453	3003480	3006915	3008376	3008453	3009303	3008749	3009607	3009710	3010979	3010441
50	Initial (nt)	2997151	2997687	2997688	2998223	2999454	3000200	3001512	3001539	3002453	3883145	3005162	3005545	3007294	3008689	3008770	3009162	3009242	3010231	3010659	3010926
	SEQ NO (a.a.)	6585	6586		6588	6889	6590	6591	6592	6593	6594	6595	9659	6597	6598	629	0099	6601	6602	6603	6604
55	SEQ NO (DNA)	3085	3086	3087	3088	3089	3090	3091	3092	3093	3094 3094	3095	3096	3097	3098	3099	3100	3101	3102	3103	3104

inosine-uridine preferring nucleoside hydrolase

317

59.3

28.4

Crithidia fasciculata iunH

Sp:IUNH\_CRIFA

903

3022998

6622 3023900

3122

DNA-3-methyladenine glycosylase

179 276

> 78.8 63.8

> 50.3 33.5

> > Alcaligenes eutrophus H16 fhp

Escherichia coli K12 tag

59.4

31.2

Streptomyces coelicolor A3(2) SCE20.08c

gp:SCE20\_8

975

flavohemoprotein

406

hypothetical membrane protein

										_										
5		Function	hypothetical protein		hypothetical protein	ısporter	sporter	metabolite transport protein homolog			succinyl-draminopimelate desuccinylase				dehydrin-like protein	maltose/maltodextrin transport ATP- binding protein		cobalt transport protein	NADPH-flavin oxidoreductase	posible preferring projection
15			hypothet		hypothet	ABC transporter	ABC transporter	metaboli			succinyl-diamii desuccinylase				dehydrin	maltose/maltod binding protein		cobalt tra	NADPH-	90.300
		Matched length (a.a.)	89		337	199	211	416			466				114	373		179	231	
20		Similarity (%)	58.0		57.9	64.8	73.0	8.79			48.5				46.0	50.1		9.79	71.4	
		identity (%)	41.0		26.1	35.7	39.3	-30.8			21.5				33.0	24.9		30.2	37.2	
25	Table 1 (continued)	Homologous gene	itis ORF 23		ophus H16	uenzae hmcB	uenzae hmcB	/deG			K12 msgB					K12 malK		lis Plasmid O cbiM	AV frp	
<i>30</i> <i>35</i>	Table 1	Homolog	Agrobacterium vitis ORF23		Alcaligenes eutrophus H16 ORF7	Haemophilus influenzae hmcB	Haemophilus influenzae hmcB	Bacillus subtilis ydeG			Escherichia coli K12 msgB				Daucus carota	Escherichia coli K12 malK		Lactococcus lactis Plasmid pNZ4000 Orf-200 cbiM	Vibrio harveyi MAV frp	
40		db Match	SP YTZ3_AGRVI		sp YGB7_ALCEU	gp:HIU68399_3	gp.HIU68399_3	pir:A69778			sp.DAPE_ECOLI				GPU DCA297422_1	sp:MALK_ECOLI		gp:AF036485_6	sp:FRP_VIBHA	
٠		ORF (bp)	285	564	1002	693	714	1209	822	687	1323	1905	774	762	954	1068	642	618	816	
45	. (7)	Terminal (nt)	3011273	3011242	3011808	3013106	3013837	3015824	3014648	3016924	3015827	3019220	3018312	3017420	3018123	3019542	3020561	3021208	3022113	
50		Initial (nt)	3010989	3011805	3012809	3013798	3014550	3014616	3015469	3016238	3017149	3017316	3017539	3018181	3019076	3020609	3021202	3021825	6621 3022928	
		SEQ NO (a.a.)	9099	9099	2099	8099	6099	0199	6611	6612	6613	6614	6615	6616	2199	6618	6619	6620	6621	:
<b>55</b>		SEQ NO (DNA)	3105	3106	3107	3108	3109	3110	3111	3112	3113	3114	3115	3116	3117	3118	3119	3120	3121	

5
10
15
20
25
30
35
40 <sub>.</sub>
45
50

	Function		oxidoreductase		transcription antiterminator or beta- glucoside positive regulatory protein		6-phospho-beta-glucosidase		6-phospho-bela-glucosidase	aspartate aminotransferase		transposase (ISCg2)	hypothetical membrane protein		UDP-glucose dehydrogenase	deoxycylidine triphosphate deaminase		hypothetical protein		beta-N-Acetylglucosamınıdase
	Matched length (a a)		210		192		167		99	402	1	401	399		442	188		229		410
	Similarity (%)		63.8		69.3		59.9		788	6 08		100.0	70.2		72.2	723		59.4		58.1
	Identity (%)		34.8		28.1		43.7		43.9	53.7		100.0	33.6		40.5	43.6		30.6		28.5
Table 1 (continued)	Homologous gene		Streptomyces coelicolor A3(2) mmyQ		Escherichia coli K12 bglC		Clostridium longisporum B6405 abgA		Clostridium longisporum B6405 abgA	Methylobacillus flagellatus aat		Corynebacterium glutamicum ATCC 13032 tnp	Streptomyces coelicolor A3(2) SCQ11.10c		Sinorhizobium meliloti rkpK	Escherichia coli K12 dcd		Streptomyces coelicolor A3(2) SCC75A, 16c		Streptomyces thermoviolaceus nagA
	db Match		gp:SCO276673_18		sp:BGLG_ECOLI		sp:ABGA_CLOLO		sp:ABGA_CLOLO	gp:L78665_2.		gp:AF189147_1	gp:SCQ11_10		prf:2422381B	sp:DCD_ECOLI		gp:SCC75A_16		gp:AB008771_1
	ORF (bp)	603	624	156	591	279	360	381	240	1257	83	1203	1257	183	1317	267	237	771	1689	1185
	Terminal (nt)	3028163	3028891	3029033	3028884	3029782	3029702	3030535	3030101	3031979	3032348	3033863	3035437	3034105	3035440	3036845	3037911	3038942	3038993	3040748
	Initial (nt)	3027561	3028268	3028878	3029474	3029504	3030061	3030155	3030340	3030723	3032647	3032661	3034181	3034287	3036756	3037411	3037675	3038172	3040681	3041932
	SEQ NO (a.a.)	6626	6627	6628	6629	6630	6631	6632	6633	6634	6635	9699	6637	6638	6639	6640	6641	6642	6643	6644
	SEQ NO. (DNA)	3126	3127	3128	3129	3130	3131	3132	3133	3134	3135	3136	3137	3138	3139	3140	3141	3142	3143	3144

Table 1 (continued)

Ī	i								. — 					ase				ŀ	Γ
	Function			hypothetical protein			hypothetical membrane protein	acyltransferase or macrolide 3-O- acyltransferase		hypothetical membrane protein		hexosyltransferase	methyl transferase	phosphoenolpyruvate carboxykinase (GTP)	C4-dicarboxylate transporter	hypothetical protein	hypothetical protein	mebrane transport protein	
	Matched length (a a)	1		1416			363	408		529		69£	251	601	332	241	207	768	
	Similarity (%)			49.4			47.1	51.0		54.8		1.67	73.3	78.5	52.7	67.2	<b>9</b> 5.0	72.3	
	Identity (%)			29.6			24.8	27.7		31.2		53.4	58.6	54.7	24.4	35.7	69.1	42.3	
(commaca)	Homologous gene		,	Mycobacterium leprae MLCB1883.13c			Mycobacterium leprae MLCB1883.05c	Streptomyces sp. acyA		Mycobacterium leprae MLCB1883.04:		Mycobacterium tuberculosis H37Rv Rv0225	Mycobacterium tuberculosis H37Rv Rv0224c	Neocallimastix frontalis pepck	Pyrococcus abyssi Orsay PAB2393	Escherichia coli K12 yggH	Mycobacterium tuberculosis H37Rv Rv0207c	Mycobacterium tuberculosis H37Rv Rv0206c mmpL3	
	db Match			gp:MLCB1883_7			gp:MLCB1883_4	pir.JC4001		gp:MLCB1883_3		pir.G70961	pir.F70961	sp.PPCK_NEOFR	pir.E75125	Sp:YGGH_ECOLI	pir.E70959	pir.C70839	
	ORF (bp)	444	201	3129	621	195	903	1068	708	1422	699	1137	177	1830	1011	765	705	2316	1422
	Terminal (nt)	3042437	3042703	3045788	3043022	3045990	3048048	3046122	3047197	3049479	3051190	3049456	3051964	3052062	3055769	3056631	3057317	3059643	3058096
	Initial (nt)	3041994	3042503	3042660	3043642	3045796	3047146	3047189	3047904	3048058	3050522	3050592	3051194	3053891	3054759	3055867	3056613	3057328	3059517
	SEQ NO (a a.)	6645	6646	6647	6648	6649	999	6651	6652	6653	6654 0034	6655	6656	2599	6658	6999	0999	6661	6662
	SEQ NO (DNA)	3145	3146	3147	3148	3149	3150	3151	3152	3153	3154	3155	3156	3157	3158	3159	3160	3161	3162

10	
15	
20	
25	
30	
35	
40	
45	

ਉ
Z E
≘
<u>ප</u>
_
<u>9</u>
a
-

	Function	hypothetical membrane protein	hypothetical membrane protein	propionyl-CoA carboxylase complex B subunit	polyketide synthase	acyl-CoA synthase	hypothetical protein		major secreted protein PS1 protein precursor				antigen 85-C	hypothetical membrane protein	nodulation protein	hypothetical protein	hypothetical protein		phosphalidic acid phosphatase
	- g	hypoth	hypoth	propionyl- B subunit		acyl-C	hypoth		major sec precursor		-		antige						
	Matched length (a a)	364	108	523	1747	592	319		657				331	199	295	168	959		170
	Similarity (%)	62.9	69.4	6.97	54.2	62.3	67.4		99.5				62.5	61.2	51.5	75.0	74.7		56.5
	Identity (%)	29.1	34.3	49.7	30.2	33.5	39.8		98.6				36.3	37.5	27.1	51.2	55.6		28.2
lable I (confined)	Homologous gene	Mycobacterium tuberculosis H37Rv Rv0204c	Mycobacterium tuberculosis H37Rv Rv0401	Streptomyces coelicolor A3(2) pccB	Streptomyces erythraeus eryA	Mycobacterium bovis BCG	Mycobacterium tuberculosis H37Rv Rv3802c		Corynebacterium glutamicum (Brevibacterium flavum) ATCC 17965 cop1				Mycobacterium tuberculosis ERDMANN RV0129C fbpC	Mycobacterium tuberculosis H37Rv Rv3805c	Azorhizobium caulinodans ORS571 noeC	Mycobacterium tuberculosis H37Rv Rv3807c	Mycobacterium tuberculosis H37Rv Rv3808c	-	Bacillus licheniformis ATCC 9945A bcrC
	db Match	pir.A70839	pir:H70633	gp.AF113605_1	sp:ERY1_SACER	prf 2310345A	pir.F70887		1971 sp.CSP1_CORGL				sp:A85C_MYCTU	pir.A70888	sp.NOEC_AZOCA	pir:C70888	pir:D70888		sp:BCRC_BACLI
	ORF (bp)	1083	363	1548	4830	1788	927	498	1971			219	1023	2058	966	504	1968	1494	477
	Terminal (nt)	3060733	3061095	3061380	3062951	3068143	3070214	3071147	3071650	7007	2012441	3073857	3075540	3076715	3078853	3079848	3080344	3083960	3083935
	Initial (nt)	3059651	3060733	3062927	3067780	3069930	3071140	3071644	3073620		3074047	3074075	3076562	3078772	3079848	3080351	3082311	3082467	6679 3084411
	SEQ NO		6664	9999	9999	2999	8999	6999	0299		/00	6672	6673	6674	6675	9299	6677	8299	629
	SEQ NO	3163	3164	3165	3166	3167	3168	3169			21.7	3172	3173	3174	3175	3176	3177	3178	3179

•	
5	
10	
15	6
20	
25	ned)
30	Table 1 (continued)
35	
40	
45	
50	

	Function			dimethylaniline monooxygenase (N- oxide-forming)		UDP-galactopyranose mutase	hypothetical protein	glycerol kinase	hypothetical protein	acyltransferase	seryl-IRNA synthetase	transcriptional regulator, GntR family or fatty acyl-responsive regulator	hypothetical protein	hypothetical protein		2,3-PDG dependent phosphoglycerate mutase		nicotinamidase or pyrazinamidase	
	Matched length (a a)			377		377	659	499	279	261	419	235	356	113		218		460	
	Similarity (%)			50.4		72.9	47.8	78.8	70.3	72.0	87.6	61.7	61.2	79.7		62.8		6.05	
	Identity (%)			24.4		43.2	29.6	51.7	41.6	46.7	70.2	27.72	32.6	46.0		37.2		27.4	
lable I (confined)	Homologous gene			Sus scrofa fmo1		Escherichia coli K12 glf	Mycobacterium tuberculosis H37Rv Rv3811 csp	Pseudomonas aeruginosa ATCC 15692 glpK	Mycobacterium tuberculosis H37Rv Rv3813c	Mycobacterium tuberculosis H37Rv Rv3816c	Mycobacterium tuberculosis H37Rv	Escherichia coli K12 farR	Mycobacterium tuberculosis H37Rv Rv3835	Mycobacterium tuberculosis H37Rv Rv3836		Amycolatopsis methanolica pgm		Mycobacterium smegmatis pzaA	
	db Match			sp:FMO1_PIG		sp.GLF_ECOLI	pir:G70520	sp.GLPK_PSEAE	pir.A70521	pir:D70521	gsp:W26465	sp. FARR_ECOLI	pir.H70652	pir.A70653		gp:AMU73808_1		prf.2501285A	
	ORF (bp)	777	510	1302	612	1203	2049	1527	834	876	1266	714	1113	342	66	699	630	1143	729
	Terminal (nt)	3084424	3085218	3087048	3088276	3087101	3090664	3090760	3092342	3093175	3094078	3096287	3097423	3097764	3097780	3097904	3099454	3100698	3101426
	Initial (nt)	3085200	3085727	3085747	3087665	3088303	3088616	3092286	3093175	3094050	3095343	3095574	3096311	3097423	3097878	3098572	3098825	3099556	3100698
	SEQ NO (a.a.)			6682	6683	6684	6685	9899	6687	6688		0699	6691	6692	6693	6694	6695	9699	2699
	SEQ NO.	3180	3181	3182	3183	3184	3185	3186	3187	3188	3189	3190	3191	3192	3193	3194	3195	3196	3197

Table 1 (continued)

	Function	transcriptional regulator				hypothetical protein	glucan 1,4-alpha-glucosidase		glycerophosphoryl diester phosphodiesterase	gluconate permease			pyruvate kinase	L-lactate dehydrogenase	hypothetical protein	hydrolase or haloacid dehalogenase-like hydrolase	efflux protein	transcription activator or transcriptional regulator GntR family	phosphoesterase	shikimate transport protein
	Matched length (a.a.)	380				107	432		259	456			491	314	526	224	188	221	255	422
	Similarity (%)	57.1				81.3	55.3		54.1	71.9			47.7	99.7	64.8	58.5	9'29	67.0	9.89	74.4
	Identity (%)	31.6				43.9	28.7		29.0	37.3	-		25.5	99.7	33.5	32.1	39.9	27.6	47.8	37.9
lable I (confinded)	Hamologous gene	Streptomyces coelicolor A3(2) SC6G4.33				Streptomyces lavendulae ORF372	Saccharomyces cerevisiae S288C YIR019C sta1		Bacillus subtilis glpQ	Bacillus subtilis gntP			Corynebacterium glutamicum AS019 pyk	Brevibacterium flavum lctA	Mycobacterium tuberculosis H37Rv Rv1069c	Streptomyces coelicolor A3(2) SC1C2.30	Brevibacterium linens ORF1 tmpA	Escherichia coli K12 MG1655 glcC	Mycobacterium tuberculosis H37Rv Rv2795c	Escherichia coli K12 shiA
	db Match	gp:SC6G4_33				pir:B26872	1314 SP. AMYH_YEAST		sp.GLPQ_BACSU	sp.GNTP_BACSU			SP.KPYK_CORGL	gsp:Y25997	pir.C70893	gp:SC1C2_30	gp.AF030288_1	sp.GLCC_ECOLI	pir:870885	sp. SHIA_ECOLI
	ORF (bp)	1035	120	552	870	327	1314	918	819	1389	842	159	1617	942	1776	636	543	693	786	1299
	Terminal (nt)	3102768	3101744	3102079	3103763	3104252	3105719	3106053	3106951	3109519	3188823	3110003	3110464	3112449	3115394	3116042	3116621	3117332	3118121	3119582
	Initial (nt)	3101734	3101863	3102630	3102894	3103926	3104406	3106970	3107769	3108131	3109464	3109845	3112080	3113390	3113619	3115407	3116079	3116640	3117336	3118284
	SEQ NO	8699	6699		6701	6702	6703	6704	6705	90/9	6707	6708	6209	6710	6711	6712	6713	6714	6715	6716
	SEQ		3199		3201	3202	3203	3204	3205	3206	3207	3208	3209	3210	3211	3212	3213	3214	3215	3216

L-lactate dehydrogenase or FMN-dependent dehydrogenase two-component system response regulator multidrug resistance transporter phosphatase or reverse transcriptase (RNA-dependent) superoxide dismutase (Fe/Mn) 5 peptidase or IAA-amino acid hydrolase peptide methionine sulfoxide membrane transport protein immunity repressor protein transcriptional regulator transcriptional regulator Function hypothetical protein 10 reductase Matched length 376 292 216 447 137 212 569 122 210 164 (a.a) 384 55 Similarity 51.3 68.9 800 63 1 69.1 92.7 65.8 49.0 64.8 593 65.0 2 % 75 Identity (%) 32.5 27.3 50.9 40.4 45.5 29.5 36.9 47.6 82.3 23.4 33.8 37.2 Streptomyces cyanogenus lanJ Corynebacterium glutamicum tetA Corynebacterium diphtheriae chrA Table 1 (continued) Bacillus phage phi-105 ORF1 Mycobacterium tuberculosis H37Rv Rv3850 Neisseria meningitidis IIdA Corynebacterium pseudodiphtheriticum sod Bacillus subtilis 168 yxaD Homologous gene Caenorhabditis elegans Y51B11A.1 Escherichia coli B msrA Arabidopsis thaliana ill1 Bacillus subtilis gttC gp:CELY51B11A\_1 sp.GLTC\_BACSU sp:YXAD\_BACSU Sp.PMSR\_ECOLI gp:AF121000\_10 Sp.ILL1\_ARATH Sp.RPC\_BPPH1 prf:2508244AB db Match prf:2219306A prf 2518330B pir.G70654 pir:140858 40 1215 1617 1134 1611 633 1491 402 456 312 651 900 924 1521 636 ORF (bp) 546 711 Ξ 150 3121909 3135268 3133778 3135752 3120879 3121313 3121992 3123932 3122556 3125495 3127494 3129739 3131395 3133030 3131508 3133747 3135856 Terminal 3124341 3124897 3125492 3126991 <u>E</u> 3126145 3133115 3135297 3125343 3126392 3119665 3122129 6721 3123222 3124172 3124886 6724 3125298 3128606 3129785 3132920 3136491 3120909 3121598 3128417 3133028 Initial <u>5</u> 6719 6725 6229 6730 6733 6734 6735 6717 6718 6722 6726 6727 6728 6731 6732 6736 6720 6723 SEQ. (a.a.) 3231 3230 3217 3218 3219 3220 3221 3232 3234 3235 (DNA) 3223 3224 3225 3226 3228 3229 3233 3227

15

20

25

30

35

45

50

10	Function			two-component system sensor histidine kinase	hypothetical protein	hypothetical protein	stage III sporulation protein	transcriptional repressor	transglycosylase-associated protein	hypothelical prolein	hypothelical protein	RNA pseudouridylate synthase	hypothetical protein	hypothetical protein		bacterial regulatory protein, gntR family or glc operon transcriptional activator	hypothetical protein	hypothetical protein
15	Matched length (a.a.)			408	48	7.7.2	265	192	87	296	314	334	84	42		109	488	267
20	Similarity (%)			64.5	79.2	59.2	53.6	6.09	71.3	69.6	73.9	51.2	0 99	75.0		26 0	48.2	78.7
	Identity (%)			30.2	45.8	30.0	26.0	32,3	34.5	41.2	38.5	28.4	61.0	71.0		30.3	26.0	48.3
25 (pg				iae	(2)51	(2)		SiS	1655	Sis	1655	bc5		66		1655		SIS
56 September 2 (Continued)	Homologous gene			Corynebacterium diphtheriae chrS	Streptomyces coelicalor A3(2) SCH69.22c	Streptomyces coelicolor A3(2) SCH69:20c	Bacillus subtilis spottlJ	Mycobacterium tuberculosis H37Rv Rv3173c	Escherichia coli K12 MG1655 tag1	Mycobacterium (uberculosis H37Rv Rv2005c	Escherichia coli K12 MG1655 yhbW	Chlorobium vibrioforme ybc5	Chlamydia pneumoniae	Chlamydia muridarum Nigg TC0129		Escherichia coli K12 MG1655 glcC	Streptomyces coelicolor SC4G6.31c	Mycobacterium tuberculosis H37Rv Rv2744c
35											1				_		=	CTU
40	db Match			prf:2518330A	gp:SCH69_22	gp:SCH69_20	sp:SP3J_BACSU	pir.C70948	sp.TAG1_ECOLI	sp.YW12_MYCTU	SP.YHBW_ECOLI	Sp. YBC5_CHLVI	GSP: Y35814	PIR: F81737		sp.GLCC_ECOLI	gp:SC4G6_31	sp.35KD_MYCTU
	ORF (bp)	639	588	1311	150	822	1302	639	261	903	987	996	273	141	207	363	1416	873
45	Terminal (nt)	3137558	3138471	3136593	3138481	3138634	3140952	3140885	3141709	3142454	3143496	3145626	3146841	3147230	3151369	3151842	3153828	3153894
50	Initial (nt)	3136920	3137884	3137903	3138630	3139455	3139651	3141523	3141969	3143356	3144482	3144661	+-	3147090	3151575		3152413	3154766
	SEO NO (a.a.)	6737	6738	6239	6740	6741	6742		6744	6745	6746	6747	$\overline{}$	<del></del>	6750		6752	6753
<i>55</i>	SEQ NO.	3237	3238	3239	3240	3241	3242	3243	3244	3245	3246	3247	3248	3249	3250	3251	3252	3253

•																 				!		
5	Function						methyltransferase	nodulin 21-related protein				transposon tn501 resolvase		ferredoxin precursor	hypothetical protein	transposase	transposase protein fragment TnpNC		glyceraldehyde-3-phosphate dehydrogenase (pseudogene)	lipoprotein	copper/potassium-transporting ATPase B or cation transporting ATPase (E1-E2 family)	
	P		-	-		<u> </u>	Ë	ě		-	_	tra	-	fer	Ě	Ē	tra Tny	-	4 g	<u>a</u>	A A Co	
15	Matched length (a.a.)						217	241				95		62	55	27	46		88	180	717	
20	Similarity (%)						58.1	55.2	,			92.9		98.4	85 5	84.0	90.0		84.2.	59.4	73.4	
	Identity (%)						32.3	26.1				48.2		90.3	47.3	81.0	84.0		63.2	32.2	45.8	
25 (juned)	Jene Jene						lor A3(2)					nosa TNP5		rythraea fer	lor A3(2)	amicum	amicum		de	C6803	IS AF0152	
% Table 1 (continued)	Homologous gene				,		Streptomyces coelicolor A3(2) SCD35, 11c	soybean NO21				Pseudomonas aeruginosa TNP5		Saccharopolyspora erythraea fer	Streptomyces coelicolor A3(2)	Corynebacterium glutamicum Tnp1673	Corynebacterium glutamicum		Pyrococcus woesei gap	Synechocystis sp. PCC6803 sll0788	Archaeoglobus fulgidus AF0152	
35			:				σσ								S					တ 🗷	_ ₹	
40	db Match	,					gp:SCD35_11	Sp. NO21_SOYBN				sp:TNP5_PSEAE		sp.FER_SACER	gp:SCD31_14	GPU:AF164956_8	GPU.AF164956_23		sp:G3P_PYRWO	pir.S77018	pir.H69268	
	ORF (bp)	153	1452	1068	249	309	711	720	204	378	186	216	483	321	333	111	162	1038	126	999	2217	171
45	Terminal (nt)	3154969	3155246	3156306	3157223	3157479	3158834	3159081	3160419	3161065	3161001	3160723	3161701	3161087	3161682	3162804	3162871	3163889	3162858	3163074	3163789	3166267
. <b>50</b>	Initial (nt)	3154817	3156697	3157373	3157471	3157787	3158124	3159800	3160216	3160688	3160816	3160938	3161219	3161407	3162014	3162694	3162710	3162852	3162983	3163733	3166005	3166437
	SEQ NO (a.a.)	6754	6755	6756	6757	6758	6529	6760	6761	6762	6763	6764	<u> </u>	99/9	6767	6768	6929	6770	6771	6772	6773	6774
55	SEQ NO (DNA)	3254	3255 (	3256	3257	3258	3259 (	3260	3261	3262	3263	3264	3265	3266	3267	3268 (	3269 6	3270 6	3271 6	3272 6	3273 6	3274 6

laccase or copper resistance protein two-component response regulator or alkaline phosphatase synthesis transcriptional regulatory protein quinone oxidoreductase (NADPH:quinone reductase)(seta-(cytochrome c biogenesis protein) thiol disulfide interchange protein zinc-transporting ATPase (Zn(II)-translocating p-type ATPase zinc-transporting ATPase (Zn(II)two-component system sensor 5 translocating p-type ATPase Function hypothetical protein histidine kinase 10 transposase precursor A transposase crystallin) 15 Matched length 233 909 (a.a) 630 101 322 30 78 72 73 70 Similarity 71.4 72.1 47.9 63.4 603 66.7 68.5 54.0 730 77.0 % 20 Identity (%) 37.5 43.4 26.7 31.7 31.4 37.2 39.8 45.0 58.0 75.0 Aeropyrum pernix K1 APE2572 Bradyrhizobium japonicum tlpA Escherichia coli K12 MG1655 atzN Corynebacterium glutamicum Tnp1673 Corynebacterium glutamıcum Tnp1673 Table 1 (continued) Synechocystis sp. PCC6803 atzN Escherichia coli K12 baeS Pseudomonas syringae pv Homologous gene Bacillus subtilis phoP Mus museulus goi tomato copA sp:PHOP\_BACSU SP.COPA\_PSESM GPU: AF164956\_8 GPU. AF164956\_8 SPIGOR MOUSE sp:ATZN\_SYNY3 SP.TLPA\_BRAJA sp:BAES\_ECOLI Sp: ATZN\_ECOLI db Match PIR:E72491 40 1875 1197 1479 918 234 390 216 ORF (bp) 756 363 258 471 315 207 309 192 672 828 3171819 3167169 3169340 3173465 3174380 3176901 Terminal 3175254 3177089 3177308 3166450 3171616 3174784 3177482 3168566 3167646 3170892 3173857 45 Ę 3177565 3172538 3173624 3174066 3174990 3166978 3167646 3167739 3168401 3168669 3169414 3171254 3172995 3175027 3175643 3177174 3177304 Initial E) 50 6775 6778 6119 6780 8782 6783 6784 6785 6786 88/9 68/9 0629 6791 27.19 6781 6787 6776 SEQ (a a.) 9 (DNA) 3285 3275 3276 3283 3284 3286 3288 3289 3278 3279 3280 3281 3282 3287 3290 3291 3277 8

25

30

35

15	
20	
25	
30	
35	
40	

Table 1 (continued)

						lable 1 (confinued)				
SEQ NO. (DNA)	SEQ NO.	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched tength (a.a.)	Function
3292	6792	3177683	3177525	159	gp:AF121000_8	Corynebacterium glutamicum 22243 R-plasmid pAG1 tnpB	92.5	96.2	53	transposase (IS1628)
3293	6793	3178558	3178112	447	sp:THI2_ECOL!	Escherichia coli K12 thi2	39.0	74.0	100	thioredoxin
3294	6794	3178609	3178872	264						
3295	6795	3179049	3180392	1344	sp:PCAK_PSEPU	Pseudomonas putida pcaK	27.1	60.1	421	transmembrane transport protein or 4-hydroxybenzoale transporter
3296	96/9	3181104	3180946	159						
3297	6797	3181126	3180551	976	sp. YQJI_ECOLI	Escherichia coli K12 yqjl	35.1	62.5	208	hypothetical protein
3298	6798	3182866	3181337	1530	sp:DNAB_ECOLI	Escherichia coli K12 dnaB	37.7	73.1	461	replicative DNA helicase
3299	6429	3183469	3183984	516						
3300	6800	3183927	3183478	450	sp:RL9_ECOLI	Escherichia coli K12 RL9	42.2	71.4	154	50S ribosomal protein L9
3301	6801	3184661	3183987	675	sp:SSB_ECOLI	Escherichia coli K12 ssb	30.6	51.5	229	single-strand DNA binding protein
3302	6802	3184985	3184701	285	sp:RS6_ECOLI	Escherichia coli K12 RS6	28.3	78.3	92	30S ribosomal protein S6
3303	6803	3185536	3185348	189						
3304	6804	3186993	3185536	1458	gp:AF187306_1	Mycobacterium smegmatis mc(2)155	41.5	68.3	480	hypothetical protein
3305	6805	3187912	3188793	882						
3306	6806	3189201	3187042	2160	sp.PBPA_BACSU	Baciflus subtilis ponA	29.1	60.1	647	penicillin-binding protein
3307	6807	3189652	3189296	357	sp:Y0HC_MYCTU	Mycobacterium tuberculosis H37Rv Rv0049	41.1	72.0	107	hypothetical protein
3308	6808	3189877	3190347	471	pir.B70912	Mycobacterium tuberculosis H37Rv Rv0042c	35.1	65.0	137	bacterial regulatory protein, marR family
3309	6889	3190378	3191319	942	sp:Y0FF_MYCTU	Mycobacterium tuberculosis H37Rv Rv2319c yofF	29.7	61.8	296	hypothetical protein
3310	6810	3191354	3191848	495						
3311	6811	3192242	3191922	321	sp:YHGC_BACSU	Bacillus subtilis yhgC	32.4	70.4	11	hypothetical protein
3312	6812	3193201	3192266	936	sp:YCEA_ECOLI	Escherichia coli K12 yceA	30.2	63.8	298	hypothetical protein
3313	6813	6813 3194514	3193252	1263	sp.YBJZ_ECOLI	Escherichia coli K12 ybjZ	31.2	64.0	433	ABC transporter ATP-binding protein

gluconokinase or gluconate kinase

486 169 159

24.5 27.8

teicoplanin resistance protein teicoplanin resistance protein

159.0 60.4 53.7

27.0

Enterococcus faecium van Z Enterococcus faecium vanZ

Bacillus subtilis gntK

1482 SP.GNTK\_BACSU

525 Sp. VANZ ENTFC 591 sp.VANZ\_ENTFC

3211246 3211904

3209705

3329 6829 3211186

																		_
5		uc	-binding protein					ng starvation	-DNA				otein-cysteine	ogenase or lase ductase) or		t protein	ise [NAD] (malic	
10		Function	ABC transporter ATP-binding protein	hypothetical protein	hypothetical protein			DNA protection during starvation protein	formamidopyrimidine-DNA glycosylase	hypothetical protein			methylated-DNAprotein-cysteine S-methyltransferase	zinc-binding dehydrogenase or quinone oxidoreductase (NADPH:quinone reductase) or alginate lyase		membrane transport protein	malate oxidoreductase [NAD] (malic enzyme)	
15	-	Matched length (a.a.)	221	237	360			154	268	404			166	231		398	392	
20		Similarity (%)	1.08	42.0	0.06			64.9	9:99	9.99			63.3	63.6		66.3	99.5	
		Identity (%)	48.9	18.0	77.8			37.7	28.4	47.5	.		38.0	33.3		26.4	99.7	L
25	inued)	ane	IG1655	2)0606	ulosis			bs	nutM or	lcB				ea pig) qor		culosis	assecola tamicum)	
30	Table 1 (continued)	Homologous gene	Escherichia coli K12 MG1655 ybj2	Campylobacter jejuni Cj0606	Mycobacterium tuberculosis H37Rv Rv0046c			Escherichia coli K12 dps	Escherichia coli K12 mutM or fpg	Escherichia coli K12 rtcB			Homo sapiens mgmT	Cavia porcellus (Guinea pig) qor		Mycobacterium tuberculosis H37Rv Rv0191 ydeA	Corynebacterium melassecola (Corynebacterium glutamicum) ATCC 17965 malE	
35				0	ΣI		<u> </u> 											
40		db Match	sp.YBJZ_ECOLI	pir.E81408	pir:F70912			sp.DPS_ECOLI	sp:FPG_ECOLI	sp.RTCB_ECOLI			sp:MGMT_HUMAN	sp.QOR_CAVPO		sp:YDEA_ECOLI	gp:AF234535_1	
		ORF (bp)	069	1977	1089	909	1485	495	813	1149	1089	573	474	1011	Ξ	1176	1176	1
45		Terminal (nt)	3194514	3195210	3198500	3198582	3199202	3201260	3202712	3204100	3202979	3204728	3204731	3205222	3206756	3208024	3209454	
50		Initial (nt)	3195203	3197186		3199187		3201754	3201900	3202952	3204067	3204156	3205204	3206232	3206646	3206849	6828 3208279	
		SEQ NO.	6814	6815	6816	6817	6818	6819	6820	6821	6822	6823	6824	6825	6826	6827		
55		SEQ	3314	3315	3316	3317	3318	3319	3320	3321	3322	3323	3324	3325	3326	3327	3328	

ned)
Ī
<u>ප</u>
Э
5

SEC	_	<del></del>			<del></del> -	- 1	<del></del>				ī							<del></del> -	
SEO   Initial   Terminal ORF   db Match   Homologous gene   (%)		Function	mercury(II) reductase	D-amino acid dehydrogenase small subunit				NAD(P)H nitroreductase			leucyl-tRNA synthetase	hypothetical membrane protein	virulence-associated protein		hypothetical protein	bifunctional protein (homoprotocatechuale catabolism bifunctional isomerase/decarboxylase) (2- hydroxyhepta-2,4-diene-1,7-dioate isomerase and 5-carboxymethyl-2- oxo-hex-3-ene-1,7dioate decarboxylase)	gentisate 1,2-dioxygenase or 1- hydroxy-2-naphthoate dioxygenase	bacterial regulatory protein, lacl family or pectin degradation repressor protein	transmembrane transport protein or 4-hydroxybenzoate transporter
SEQ   Initial   Terminal   ORF   db Match   Homologous gene   (%)   (m1)   (hp)   (h		Matched length (a.a.)	448	444				194			943	104	96		247	298	339	229	454
SEQ   Initial   Terminal   ORF   db Match   Homologous gene   NO   (III)   (		Similarity (%)	65.6	54.5				55.2			68.1	40.4	81.4		53.8	50.3	64.3	60.7	8.09
SEQ Initial Terminal ORF db Match (a a ) (nt) (nt) (nt) (bp) db Match (a a ) (nt) (nt) (bp) db Match (a a ) (a a ) (a 2)		Identity (%)	29.9	27.3				25.8			47.7	40.4	55.8		31.6	28.5	34.2	25.3	27.5
SEQ (nt) (nt) (nt) (nt) (nt) (a a y) (a 1) (nt) (nt) (nt) (nt) (nt) (nt) (nt) (nt	lable 1 (continued)	Homologous gene	Staphylococcus aureus merA	Escherichia coli K12 dadA				Thermus thermophilus nox			Bacillus subtilis syl	Escherichia coli K12	Dichelobacter nodosus vapl		Streptomyces coelicolor SCC54.19	Escherichia coli K12 hpcE	Pseudomonas alcaligenes xInE		Pseudomonas putida pcaK
SEQ (nt) (nt) (nt) (nt) (a a b) (a a b) (nt) (nt) (nt) (nt) (a a b) (a a c) (a a c) (a c)		db Match	Sp.MERA_STAAU	sp.DADA_ECOLI				sp:NOX_THETH			sp:SYL_BACSU	sp.YBAN_ECOLI	SP VAPI_BACNO	-	gp:SCC54_19	sp:HPCE_ECOLI	gp:AF173167_1	sp.KDGR_ERWCH	sp.PCAK_PSEPU
SEO   Initial   NO   (II)   (I		ORF (bp)	1344	1230	1503	330	321	609	924	1452	2856	429	357	774	723	837	1125	780	1356
SEQ SEQ (nt) (nt) (DNA) (a a) (nt) (a b) (nt) (a b) (nt) (a b) (nt) (a b		Terminal (nt)	3213931	3213934	3215257	3216886	3217457	3218601	3219700	3222495	3219778	3223150	3223089	3225374	3223992	3224718	3225563	3226910	3229079
SEQ SEQ NO NO NO NO NO NO NO NO NO NO NO NO NO		Initial (nt)	3212588	3215163		3217215	321777	3217993	3218777	3221044	3222633	3222722	1		3224714	3225554			3227724
SEQ NO NO NO NO NO NO NO NO NO NO NO NO NO		SEQ NO (a a)	6832							6839	6840	6841	6842	6843	6844	6845	6846	6847	6848
							_	_	_	_			_	_	*	3345	3346		3348

_	· 1					-	F	1			<del></del> -				<u> </u>	
	Function	salicylate hydroxylase	proton/glutamate symporter or excitatory amino acid transporter2	tryptophan-specific permease	anthranilate synthase component I		anthranilate synthase component II	anthranilate phosphoribosyltransferase	indole-3-glycerol phosphate synthase (IGPS) and N-(5- phosphoribosyl) anthranilate isomerase(PRAI)		tryptophan synthase beta chain	tryptophan synthase alpha chain	hypothetical membrane protein	PTS system, IIA component or unknown pentitol phosphotransferase enzyme II, A component	ABC transporter ATP-binding protein	ABC transporter
	Matched length (a a)	476	507	170	515		208	348	474		417	283	521	152	305	547
	Similarity (%)	49.4	54.4	99.4	9.66		100.0	99.4	98.3		97.9	96 5	8.98	71.7	63.6	57.2
	Identity (%)	28.2	25.4	99.4	99.2		0.66	99.4	97.3		9.76	95.4	9.99	30.3	32.5	25.2
Table 1 (continued)	Homologous gene	Pseudomonas putida	Homo sapiens eat2	Corynebacterium glutamicum AS019 ORF1	Brevibacterium lactofermentum trpE		Brevibacterium lactofermentum trpG	Corynebacterium glutamicum ATCC 21850 trpD	Brevibacterium lactofermentum trpC	-	Brevibacterium lactofermentum trpB	Brevibacterium lactofermentum trpA	Streptomyces coelicolor A3(2) SCJ21.17c	Escherichia coli K12 ptxA	Pseudomonas stutzeri	Streptomyces coelicolor A3(2) SCH10 12
	db Match	prf:1706191A	sp:EAT2_HUMAN	pir.JC2326	sp.TRPE_BRELA		TRPG_BRELA	sp.TRPD_CORGL	sp.TRPC_BRELA		Sp.TRPB_BRELA	sp.TRPA_BRELA	gp.SCJ21_17	sp.PTXA_ECOLI	sp:NOSF_PSEST	gp:SCH10_12
	ORF (bp)	1326	1251	510	1554	171	624	1044	1422	969	1251	840	1539	810	906	1584
	Terminal (nt)	3230444	3231054	3233105	3234956	3233250	3235579	3236645	3238062	3236518	3239332	3240171	3240313	3241879	3243759	3245342
	Initial (nt)	3229119		3232596	3233403	3233420	3234956	3235602	3236641	3237213	3238082	3239332	3241851	3242688	3242854	3243759
	SEQ NO.	6849	6850	6851	6852	6853	6854	6855	9589	6857	6858	6889	6860	6861	6862	6863
	SEQ NO.	3349	3350	3351	3352	3353	3354	3355	3356	3357	3358	3359	3360	3361	3362	3363

5		Function	cytchrome b6-F complex iron-sulfur subunit (Rieske iron-sulfur protein)	NADH oxidase or NADH-dependent flavin oxidoreductase	hypothetical membrane protein	hypothetical protein	bacterial regulatory protein, arsR family or methylenomycin A resistance protein	NADH oxidase or NADH-dependent flavin oxidoreductase	hypothetical protein				** **	acetoin(diacetyl) reductase (acetoin dehydrogenase)	hypothetical protein	di-/Iripeptide transpoter		bacterial regulatory protein, tetR family	hydroxyquinol 1,2-dioxygenase
15	j	Matched length (a.a.)	305	336	328	262	102	347	226					238	58	469		188	246
20		Similarity (%)	63.6	64.3	74.7	54.6	79.4	64.3	69.5					52.9	84.5	71.6		50.5	62.2
		Identity (%)	32.5	33.3	43.6	34.0	45.1	33.4	31.4					26.9	53.5	34.5		26.1	31.7
25	Table 1 (continued)	is gene	a petC	ter brockii	12 yfeH	icolor A3(2)	icolor Plasmid	ter brockii	erevisiae					budC	erculosis	subsp. lactis		2 acrR	oaceticus
30	Table 1 (c	Homologous gene	Chlorobium limicola petC	Thermoanaerobacter brockii nadO	Escherichia coli K12 yfeH	Streplomyces coelicolor A3(2) SCI11.36c	Streptomyces coelicolor Plasmid SCP1 mmr	Thermoanaerobacter brockii nadO	Saccharomyces cerevisiae ymyO		,			Klebsiella terrigena budC	Mycobacterium tuberculosis H37Rv Rv2094c	Lactococcus lactis subsp. lactis dfpT		Escherichia coli K12 acrR	Acinetobacter calcoaceticus catA
35		db Match																	
40		db A	sp.UCRI_CHLLT	sp:NADO_THEBR	SP.YFEH_ECOLI	gp:SCI11_36	pir.A29606	SP:NADO_THEBR	Sp.YMY0_YEAST					sp:BUDC_KLETE	sp:YY34_MYCTU	sp:DTPT_LACLA		SP. ACRR_ECOLI	sp.CATA_ACICA
		ORF (bp)	450	1110	972	774	348	1092	648	153	192	168	321	753	180	1359	171	555	903
45		Terminal (nl)	3245766	3245822	3248205	3249165	3249187	3250742	3251405	3251466	3251743	3252133	3252316	3253480	3253739	3253824	3255719	3255744	3256471
50		Initial (nt)	3245317	3246931	3247234	3248392	3249534	3249651	3250758	3251618	3251934	3252300	3252636	3252728	3253560	3255182	3255549	3256298	3257373
		SEQ NO. (a.a.)	6864	6865	9989	6867	6868	6989	6870	6871	6872	6873	6874	6875	6876	6877	6878	6879	6880
55		SEQ NO (DNA)	3364	3365	3366	3367	3368	3369	3370	3371	3372	3373	3374	3375	3376	3377	3378	3379	3380

								_		_				_			_				
5		Function	eductase	sugar transporter or D-xylose-proton symporter (D-xylose transporter)	bacterial transcriptional regulator or acetate operon repressor		nent protein	lehydrogenase	dehydrogenase or myo-inositol 2- dehydrogenase or streptomycin biosynthesis protein	se						DEAD box RNA helicase family	mbrane protein		phosphomethylpyrimidine kinase	mercuric ion-binding protein or heavy-metal-associated domain containing protein	uptake protein
10		J.F.	maleylacetate reductase	sugar transporte symporter (D-xy	bacterial transcriptional re acetate operon repressor	oxidoreductase	diagnostic fragment protein sequence	myo-inositol 2-dehydrogenase	dehydrogenase or m dehydrogenase or st biosynthesis protein	phosphoesterase				stomatin		DEAD box RNA	hypothetical membrane protein		phosphomethyl	mercuric ion-binding protein or heavy-metal-associated domai containing protein	ectoine/proline uptake protein
15		Matched length (a.a.)	351	513	280	357	270	332	343	1242				206		1660	141		125	29	767
20		Similarity (%)	75.5	58.3	60.7	55.7	58.2	59.6	62.4	62.7				57.3		80.2	61.0		8.97	70 1	62.3
		Identity (%)	43.0	31.4	25.7	27.2	25.9	26.5	34.1	33.3				28.6		58.4	34.8		50.4	46.3	29.9
25	Table 1 (continued)	us gene	P51	12 xylE	nurium icIR	12 ydgJ	train 4450	eliloti idhA	eus stri	/nB				egans unc1		ovis BCG	prae u2266k		Q.	/g/	glutamicum
30	Table 1 (	Homologous gene	Pseudomonas sp. P51	Escherichia coli K12 xylE	Salmonella typhimurium iclR	Escherichia coli K12 ydgJ	Listeria innocua strain 4450	Sinorhizobium meliloti idhA	Streptomyces griseus stri	Bacillus subtilis yvnB				Caenorhabditis elegans unc1		Mycobacterium bovis BCG RvD1-Rv2024c	Mycobacterium leprae u2266k		Bacillus subtilis thiD	Bacillus subtilis yvgY	Corynebacterium glutamicum proP
35										ω.							_			- 8	
40		db Match	SP. TCBF_PSESQ	sp:XYLE_ECOLI	sp:ICLR_SALTY	sp:YDGJ_ECOLI	gsp:W61761	sp:MI2D_BACSU	sp.STRI_STRGR	pir:C70044	;			Sp.UNC1_CAEEL		gp:MBO18605_3	prf:2323363AAM		sp.THID_BACSU	pir.F70041	prf.2501295A
		ORF (bp)	1089	1524	861	1077	879	1005	1083	4032	645	618	1086	744	696	4929	207	360	900	243	837
45		Terminal (nt)	3257403	3258561	3261989	3263221	3264115	3265146	3266266	3271093	3267913	3268618	3272477	3274488	3275602	3276671	3281666	3283101	3282347	3283383	3283473
50		Initial (nt)	3258491	3260084	3261129	3262145	3263237	3264142	3265184	3267062	3268557	3269235	3271392	3275231	3276570	3281599	3282172	3282742	3282946	3283141	3284309
		SEQ NO.	6881	6882	6883	6884	6885	9889	6887	6888	6889	6890	6891	6892	6893	6894	6895	9689	2689	8689	6689
55		SEQ NO.	3381		3383	3384	3385	3386	3387	3388	3389	3390	3391	3392	3393	3394	3395	3396	3397	3398	3399

55		50	45		35 40	25 30		20	15	5
						Table 1 (continued)				
SEQ NO.	SEQ NO.	Initial (nt)	Terminal (nt)	ORF (bp)	db Match	Homologous gene	Identity (%)	Similarity (%)	Matched tength (a a)	Function
3400	0069	3285355	3284399	957	sp.FECB_ECOU	Escherichia coli K12 fecB	29.4	9.09	279	iron(III) dicitrate-binding periplasmic protein precursor or iron(III) dicitrate transport system permease protein
3401	6901	3285455	3286576	1122	sp:MRF1_SCHPO	Schizosaccharomyces pombe mrf1	27.2	58.0	324	mitochondrial respiratory function protein or zinc-binding dehydrogenase or NADPH quinone oxidoreductase
3402	6902	3286622	3287005	384						
3403	6903	3287297	3287079	219						
3404	6904	3288190	3287393	798	sp.THID_BACSU	Bacillus subtilis thiD	46.2	75.5	249	phosphomethylpyrimidine kinase
3405	6905	3288265	3288609	345						
3406	9069	3288685	3288885	201	pir:F70041	Bacillus subtilis yvgY	41.8	70.1	29	mercuric ion-binding protein or heavy-metal-associated domain containing protein
3407	6907	3289315	3288971	345	sp:AZLD_BACSU	Bacillus subtilis azID	36.3	65.7	102	branched-chain amino acid transport
3408	8069	3290021	3289311	711	sp:AZLC_BACSU	Bacillus subtilis azID	32.1	67.0	212	branched-chain amino acid transport
3409	6069	3290591	3290025	267	sp:YQGE_ECOLI	Escherichia coli K12 yqgE	23.7	56.2	169	hypothetical protein
3410	6910	3291942	3290623	1320	sp:CCA_ECOLI	Escherichia coli K12 cca	26.8	51.8	471	IRNA nucleotidyltransferase
3411	6911	3292532	3293497	996	pir.E70600	Mycobacterium tuberculosis H37Rv Rv3908	43.6	69.2	234	mutator mutT protein
3412	6912	3292882	3292610	273						
3413	6913	3293497	3296007	2511	pir:F70600	Mycobacterium tuberculosis H37Rv Rv3909	25.8	54 3	858	hypothetical membrane protein
3414	6914	3296156	3299404	3249	pir:G70600	Mycobacterium tuberculosis H37Rv Rv3910	35.7	60.1	1201	hypothetical membrane protein
3415	6915	3297706	3298428	723						
3416	6916	3299661	3300263	603	sp:RPSH_PSEAE	Pseudomonas aeruginosa algU	30.2	6.09	189	RNA polymerase sigma-H factor or sigma-70 factor (ECF subfamily)
3417	6917	3300371	3301321	951	Sp.TRXB_STRCL	Streptomyces clavuligerus txB	60.4	82.5	308	thioredoxin reductase

-	5
	10
	15
	20 <sub>.</sub>
	<b>25</b>
	<i>30</i>
	35
	40
	45
	50

	Function		thioredoxin ch2, M-type	N-acetylmuramoyl-L-alanine amidase			hypothetical protein	hypothetical protein	partitioning or sporulation protein	glucose inhibited division protein B	hypothetical membrane protein	ribonuclease P protein component	50S ribosomal protein L34			L-aspartate-alpha-decarboxylase precursor	2-isopropylmalate synthase	hypothetical protein	aspartate-semialdehyde dehydrogenase	3-dehydroquinase
	Matched length (a.a.)		119	196			212	367	272	153	313	123	47			136	616	85	344	149
	Similarity (%)		76.5	75.4			58.5	60.5	78.0	64.7	75.4	59.4	93.6			100.0	100.0	100.0	100.0	100.0
	Identity (%)		42.0	51.0			34.4	37.6	0.29	36.0	44.7	26.8	83.0			100.0	100.0	100.0	100.0	100.0
Table 1 (continued)	Homologous gene		Chiamydomonas reinhardtii thi2	Bacillus subtilis cwlB			Mycobacterium tuberculosis H37Rv Rv3916c	Pseudomonas putida ygi2	Mycobacterium tuberculosis H37Rv parB	Escherichia coli K12 gidB	Mycobacterium tuberculosis H37Rv Rv3921c	Bacillus subtilis rnpA	Mycobacterium avium rpmH		•	Corynebacterium glutamicum panD	Corynebacterium glutamicum ATCC 13032 leuA	Corynebacterium glutamicum (Brevibacterium flavum) ATCC 13032 orfX	Corynebacterium glutamicum asd	Corynebacterium glutamicum ASO19 aroD
-	db Match		Sp.THI2_CHLRE	sp.cwlB_BACSU			pir:D70851	sp:YGI2_PSEPU	sp:YGI1_PSEPU	sp GIDB_ECOLI	pir:A70852	sp.RNPA_BACSU	gp:MAU19185_1			gp:AF116184_1	sp:LEU1_CORGL	sp:YLEU_CORGL	sp:DHAS_CORGL	gp.AF124518_1
	ORF (bp)	1185	372	1242	111	1041	618	1152	837	699	951	399	336	294	222	408	1848	255	1032	447
	Terminal (nt)	3300119	3301729	3302996	3301989	3304475	3302999	3303636	3304835	3305864	3306682	3307971	3308412	3309321	3308822	147573	266154	268814	271691	446521
	tnitial (nt)	3301303	3301358	3301755	3302765	3303435	3303616	3304787	3305671	3306532	3307632	3308369	3308747	3309028	3309043	147980	268001	269068	270660	446075
	SEQ NO. (a.a.)	6918	6919	6920	6921	6922	6923	6924	6925	9269	6927	6928	6269	6930	6931	6932	6933	6934	6935	6936
	SEQ NO (DNA)	3418	3419	3420	3421	3422	3423	3424	3425	3426	3427	3428	3429	3430	3431	3432	3433	3434	3435	3436

				,		,							_		
	Function	elongation factor Tu	preprotein translocase secY subuit	isocitrate dehydrogenase (oxalosuccinatedecarboxylase)	acyl-CoA carboxylase or biotin- binding protein	citrate synthase	putative binding protein or peptidyl- prolyl cis-trans isomerase	glycine betaine transporter	hypothetical membrane protein	L-lysine permease	aromatic amino acid permease	hypothetical protein	succinyl diaminopimelate desuccinylase	proline transport system	arginyl-tRNA synthelase
	Matched length (a.a.)	396	440	738	591	437	118	595	426	501	463	316	369	524	550
	Similarity (%)	100.0	100 0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Identity (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Table 1 (continued)	Homologous gene	Corynebacterium glutamicum ATCC 13059 tuf	Corynebacterium glutamicum (Brevibacterium flavum) MJ233 secY	Corynebacterium glutamicum ATCC 13032 icd	Corynebacterium glutamicum ATCC 13032 accBC	Corynebacterium glutamicum ATCC 13032 gltA	Corynebacterium glutamicum ATCC 13032 RbA	Corynebacterium glutamicum ATCC 13032 betP	Corynebacterium glutamicum ATCC 13032 orf2	Corynebacterium glutamicum ATCC 13032 lysl	Corynebacterium glutamicum ATCC 13032 aroP	Corynebacterium glutamicum ATCC 13032 orf3	Corynebacterium glutamicum ATCC 13032 dapE	Corynebacterium glutamicum ATCC 13032 putP	Corynebacterium glutamicum AS019 ATCC 13059 argS
	db Match	sp:EFTU_CORGL	sp SECY_CORGL	sp:IDH_CORGL	pri:2223173A	sp.CISY_CORGL	sp.FKBP_CORGL	sp:BETP_CORGL	sp:YLI2_CORGL	1503 sp:LYSI_CORGL	sp.AROP_CORGL	pir.S52753	prf 2106301A	gp:CGPUTP_1	sp:SYR_CORGL
	ORF (bp)	1188	1320	2214	1773	1311	354	1785	1278	1503	1389	948	1107	1572	1650
	Terminal (nt)	527563	570771	677831	718580	879148	879629	946780	1029006	1030369	1153295	1154729	1156837	1218031	1239923
	Initial (nt)	526376	569452	680044	720352	877838	879276	944996	1030283	1031871	1154683	1155676	1155731	1219602	1238274
	SEQ NO. (a.a.)	6937	6938	6839	6940	6941	6942	6943	6944	6945	6946	6947	6948	6949	0569
	SEQ NO (DNA)	3437	3438	3439	3440	3441	3442	3443	3444	3445	3446	3447	3448	3449	3450

5		Function	diaminopimelate (DAP) decarboxylase (meso- diaminopimelate decarboxylase)	homoserine dehydrogenase	homoserine kinase	ion channel subunit	lysine exporter protein	lysine export regulator protein	acetohydroxy acid synthase, large subunit	acetohydroxy acid synthase, small subunit	acetohydroxy acid isomeroreductas	3-isopropylmalate dehydrogenase	PTS system, phosphoenolpyruvate sugar phosphotransferase (mannose and glucose transport)	acetylglutamale kinase	ornithine carbamoyltransferase	arginine repressor
15		hed Jth				-						i				
		Matched length (a.a.)	445	445	309	216	236	290	929	172	338	340	683	294	319	171
20		Similarity (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
		Identity (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
25	Table 1 (continued)	ns gene	glutamicum 159 lysA	glutamicum 159 hom	glutamicum 159 thrB	glutamicum	glutamicum	glutamicum	glutamicum	glutamicum	glutamicum	glutamicum	glutamicum	glutamicum 3	glutamicum	glutamicum
30	Table 1 (	Homologous gene	Corynebacterium glutamicum AS019 ATCC 13059 lysA	Corynebacterium glutamicum AS019 ATCC 13059 hom	Corynebacterium glutamicum AS019 ATCC 13059 thrB	Corynebacterium glutamicum R127 orf3	Corynebacterium glutamicum R127 lysE	Corynebacterium glutamicum R127 lysG	Corynebacterium ATCC 13032 ilvB	Corynebacterium glutamicum ATCC 13032 ilvN	Corynebacterium glutamicum ATCC 13032 ilvC	Corynebacterium glutamicum ATCC 13032 leuB	Corynebacterium glutamicum KCTC1445 ptsM	Corynebacterium glutamicum ATCC 13032 argB	Corynebacterium glutamicum ATCC 13032 argF	Corynebacterium glutamicum ASO19 argR
35 40		db Match	sp.DCDA_CORGL	sp.DHOM_CORGL	sp:KHSE_CORGL	gsp:W37716	sp.LYSE_CORGL	sp:LYSG_CORGL	sp.ILVB_CORGL	pir:B48648	pir.C48648	sp.LEU3_CORGL	prf.2014259A	SP. ARGB_CORGL	sp.OTCA_CORGL (	gp:AF041436_1
70		H 6	1335 sp.				-									
		ORF (bp)	i	1 1335	1 927	3 627	3 708	4 870	8 1878	3   516	7 1014	1020	5 2049	2 882,	1 957	513
45	-	Termina (nt)	1241263	1243841	1244781	1328243	1328246	1329884	1340008	1340540	1341737	1354508	1425265	1467372	1469521	1470040
50		Initial (nt)	1239929	1242507	1243855	1327617	1328953	1329015	1338131	1340025	1340724	1353489	1423217	1466491	1468565	1469528
		SEQ NO.	6951	6952	6953	6954	6955	9569	6957	8569	6929	0969	6961	6962	6963	6964
		SEQ NO.	3451	3452	3453	3454	3455	3456	3457	3458	3459	3460	3461	3462	3463	3464

5		e	Ð	oxylase	otein, high	ane protein	carboxylase	(5- 3-phosphate	1Se	oolymerase	itein		nthase	ductase	ase (acceptor)
10	Function	NADH dehydrogenase	phosphoribosyl-ATP- pyrophosphohydrolase	ornithine-cyclodecarboxylase	ammonium uptake protein, high affinity	protein-export membrane protein secG	phosphoenolpyruvate carboxylase	chorismate synthase (5- enolpyruvylshikimate-3-phosphate phospholyase)	restriction endonuclease	sigma factor or RNA polymerase transcription factor	glutamate-binding protein	recA protein	dihydrodipicolinate synthase	dihydrodipicolinate reductase	L-malate dehydrogenase (acceptor)
15	Matched length (a.a.)	467	87	362	452	77	919	410	632	331	295	376	301	248	200
20	Similarity (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Identity (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
25 Q	je je	nicum	nicum	nicum	nicum	nicum	nicum	nicum	nicum	nicum	nicum	nicum	nicum mentum)	nicum mentum)	nicum
30 Table 1 (continued)	Homologous gene	Corynebacterium glutamicum ATCC 13032 ndh	Corynebacterium glutamicum ASO19 hisE	Corynebacterium glutamicum ATCC 13032 ocd	Corynebacterium glutamicum ATCC 13032 amt	Corynebacterium glutamicum ATCC 13032 secG	Corynebacterium glutamicum ATCC 13032 ppc	Corynebacterium glutamicum AS019 aroC	Corynebacterium glutamicum ATCC 13032 cgllIR	Corynebacterium glutamicum ATCC 13869 sigB	Corynebacterium glutamicum ATCC 13032 gluB	Corynebacterium glutamicum AS019 recA	Corynebacterium glutamicum (Brevibacterium lactofermentum) ATCC 13869 dapA	Corynebacterium glutamicum (Brevibacterium lactofermentum) ATCC 13869 dapB	Corynebacterium glutamicum R127 mqo
35	db Match	gp:CGL238250_1	gp.AF086704_1	gp.CGL007732_4	gp.CGL007732_3	gp:CGL007732_2	prf:1509267A	gp.AF124600_1	pir:855225	prf.2204286D	sp:GLUB_CORGL	sp.RECA_CORGL	sp:DAPA_BRELA	sp:DAPB_CORGL	gp.CGA224946_1
	ORF (bp)	1401	261	1086	1356	231	2757	1230	1896	993	885	1128	. 903	744	1500
45	Terminal (nt)	1543154	1586465	1674123	1675268	1677049	1677387	1719669	1882385	2021846	2061504	2063989	2079281	2081191	2113864
50	Initial (nt)	1544554	1586725	1675208	1676623	1677279	1680143	1720898	1880490	2020854	2060620	2065116	2080183	2081934	2115363
	SEQ NO		9969	2969	6968	6969	0269	6971	6972	6973	6974	6975	9269	7.69	6978
5 <b>5</b>	SEQ NO.	3465	3466	3467	3468	3469	3470	3471	3472	3473	3474	3475	3476	3477	3478

,	<del></del>															
	Function	uridilylytransferase, uridilytyl- removing enzyme	nitrogen regulatory protein P-II	ammonium transporter	glutamate dehydrogenase (NADP+)	pyruvate kinase	glucokinase	glutamine synthetase	threonine synthase	ectoine/proline/glycine betaine carrier	malate synthase	isocitrate lyase	glutamate 5-kinase	cystathionine gamma-synthase	ribonucleotide reductase	glutaredoxin
	Matched length (a a)	692	112	438	447	475	323	477	481	615	739	432	369	386	148	11
	Similarity (%)	100 0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Identity (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Table 1 (continued)	Homologous gene	Corynebacterium glutamicum ATCC 13032 glnD	Corynebacterium glutamicum ATCC 13032 glnB	Corynebacterium glutamicum ATCC 13032 amtP	Corynebacterium glutamicum ATCC 17965 gdhA	Corynebacterium glutamicum AS019 pyk	Corynebacterium glutamicum ATCC 13032 glk	Corynebacterium glutamicum ATCC 13032 glnA	Corynebacterium glutamicum thrC	Corynebacterium glutamicum ATCC 13032 ectP	Corynebacterium glutamicum ATCC 13032 aceB	Corynebacterium glutamicum ATCC 13032 aceA	Corynebacterium glutamicum ATCC 17965 proB	Corynebacterium glutamicum ASO19 metB	Corynebacterium glutamicum ATCC 13032 nrdl	Corynebacterium glutamicum ATCC 13032 nrdH
	db Match	gp:CAJ10319_4	gp:CAJ10319_3	gp:CAJ10319_2	pir:S32227	1425 SP:KPYK_CORGL	gp:AF096280_1	prf.2322244A	sp:THRC_CORGL	prf.2501295B	pir:140715	pir:140713	sp:PROB_CORGL	gp:AF126953_1	gp:AF112535_2	gp:AF112535_1
	ORF (bp)	2076	336	1314	1341	1425	696	1431	1443	1845	2217	1296	1107	1158	444	231
	Terminal (nt)	2169666	2171751	2172154	2194742	2205668	2316582	2350259	2353600	2448328	2467925	2472035	2496670	2590312	2679684	2680419
	Initial (nt)	2171741	2172086	2173467	2196082	2207092	2317550	2348829	2355042	2450172	2470141	2470740	2497776	2591469	2680127	2680649
	SEQ NO (a a.)	6269	0869	6981	6982	6983	6984	6985	9869	2869	6988	6869	0669	6991	6992	6993
	SEQ NO (DNA)	3479	3480	3481	3482	3483	3484	3485	3486	3487	3488	3489	3490	3491	3492	3493

							y	Ī	
	Function	meso-diaminopimelate D- dehydrogenase	porin or cell wall channel forming protein	acetate kinase	phosphate acetyltransferase	multidrug resistance protein or macrolide-efflux pump or drug:proton antiporter	ATP-dependent protease regulatory subunit	prephenate dehydratase	ectoine/proline uptake protein
	Matched length (a.a.)	320	45	397	329	459	852	315	504
	Identity Similarity Matched (%) (%) (aa)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Identity (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Table 1 (continued)	Homologous gene	Corynebacterium glutamicum KY10755 ddh	Corynebacterium glutamicum MH20-22B porA	Corynebacterium glutamicum ATCC 13032 ackA	Corynebacterium glutamicum ATCC 13032 pta	Corynebacterium glutamicum ATCC 13032 cmr	Corynebacterium glutamicum ATCC 13032 clp8	Corynebacterium glutamicum pheA	Corynebacterium glutamicum ATCC 13032 proP
	db Match	sp:DDH_CORGL	35 gp.CGL238703_1	191 sp:ACKA_CORGL	prf.2516394A	1377 prf.2309322A	2556 sp:CLPB_CORGL	945 prf 1210266A	1512 prf 2501295A
	ORF (bp)	096	135	1191	987	1377	2556	945	1512
	Terminal (nt)	2786756	2887944	2935315	2936508	2962718	2963606	3098578	3272563
	Initial (nt)	2787715	2888078	2936505	2937494	2961342	2966161	3099522	3501 7001 3274074
	SEQ NO.		6995	9669	7669	8669	6669	7000	7001
	SEQ NO (DNA)	3494	3495	3496	3497	3498	3499	3500	3501

5

## Example 2

10

15

25

30

40

45

Determination of effective mutation site

(1) Identification of mutation site based on the comparison of the gene nucleotide sequence of lysine-producing B-6 strain with that of wild type strain ATCC 13032

[0374] Corynebacterium glutamicum B-6, which is resistant to S-(2-amino thyl)cysteine (AEC), rifampicin, streptomycin and 6-azauracil, is a lysine-producing mutant having been mutated and bred by subjecting the wild type ATCC 13032 strain to multiple rounds of random mutagenesis with a mutagen, N-methyl-N' -nitro-N-nitrosoguanidine (NTG) and screening (Appl. Microbiol. Biotechnol., 32: 269-273 (1989)). First, the nucleotide sequences of genes derived from the B-6 strain and considered to relate to the lysine production were determined by a method similar to the above. The genes relating to the lysine production include lysE and lysG which are lysine-excreting genes; ddh, dapA, hom and IysC (encoding diaminopimelate dehydrogenase, dihydropicolinate synthase, homoserine dehydrogenase and aspartokinase, respectively) which are lysine-biosynthetic genes; and pyc and zwf (encoding pyruvate carboxylase and glucose-6-phosphate dehydrogenase, respectively) which are glucose-metabolizing genes. The nucleotide sequences of the genes derived from the production strain were compared with the corresponding nucleotide sequences of the ATCC 13032 strain genome represented by SEQ ID NOS:1 to 3501 and analyzed. As a result, mutation points were observed in many genes. For example, no mutation site was observed in lysE, lysG. ddh, dapA, and the like, whereas amino acid replacement mutations were found in hom, lysC, pyc, zwf, and the like. Among these mutation points, those which are considered to contribute to the production were extracted on the basis of known biochemical or genetic information. Among the mutation points thus extracted, a mutation, Val59Ala, in hom and a mutation, Pro458Ser, in pyc were evaluated whether or not the mutations were effective according to the following method.

(2) Evaluation of mutation, Val59Ala, in hom and mutation, Pro458Ser, in pyc

[0375] It is known that a mutation in hom inducing requirement or partial requirement for homoserine imparts lysine productivity to a wild type strain (*Amino Acid Fermentation*, ed. by Hiroshi Aida *et al.*, Japan Scientific Societies Press). However, the relationship between the mutation, Val59Ala, in *hom* and lysine production is not known. It can be examined whether or not the mutation, Val59Ala, in *hom* is an effective mutation by introducing the mutation to the wild type strain and examining the lysine productivity of the resulting strain. On the other hand, it can be examined whether or not the mutation, Pro458Ser, in *pyc* is effective by introducing this mutation into a lysine-producing strain which has a deregulated lysine-bioxynthetic pathway and is free from the *pyc* mutation, and comparing the lysine productivity of the resulting strain with the parent strain. As such a lysine-producing bacterium, No. 58 strain (FERM BP-7134) was selected (hereinafter referred to the "lysine-producing No. 58 strain" or the "No. 58 strain"). Based on the above, it was determined that the mutation, Val59Ala, in *hom* and the mutation, Pro458Ser, in *pyc* were introduced into the wild type strain of *Corynebacterium glutamicum* ATCC 13032 (hereinafter referred to as the "wild type ATCC 13032 strain" or the "ATCC 13032 strain") and the lysine-producing No. 58 strain, respectively, using the gene replacement method. A plasmid vector pCES30 for the gene replacement for the introduction was constructed by the following method.

[0376] A plasmid vector pCE53 having a kanamycin-resistant gene and being capable of autonomously replicating in Coryneform bacteria (*Mol. Gen. Genet., 196.* 175-178 (1984)) and a plasmid pMOB3 (ATCC 77282) containing a levansucrase gene (*sacB*) of *Bacillus subtilis* (*Molecular Microbiology, 6:* 1195-1204 (1992)) were each digested with *Pst*l. Then, after agarose gel electrophoresis, a pCE53 fragment and a 2.6 kb DNA fragment containing *sacB* were each extracted and purified using GENECLEAN Kit (manufactured by BIO 101). The pCE53 fragment and the 2.6 kb DNA fragment were ligated using Ligation Kit ver. 2 (manufactured by Takara Shuzo), introduced into the ATCC 13032 strain by the electroporation method (*FEMS Microbiology Letters,* 65: 299 (1989)), and cultured on BYG agar medium (medium prepared by adding 10 g of glucose, 20 g of peptone (manufactured by Kyokuto Pharmaceutical), 5 g of yeast extract (manufactured by Difco), and 16 g of Bactoagar (manufactured by Difco) to 1 liter of water, and adjusting its pH to 7.2) containing 25 µg/ml kanamycin at 30°C for 2 days to obtain a transformant acquiring kanamycin-resistance. As a result of digestion analysis with restriction enzymes, it was confirmed that a plasmid extracted from the resulting transformant by the alkali SDS method had a structure in which the 2.6 kb DNA fragment had been inserted into the *Pst*l site of pCE53. This plasmid was named pCES30.

[0377] Next, two genes having a mutation point, hom and pyc, were amplified by PCR, and inserted into pCES30 according to the TA cloning method (Bio Experiment Illustrated vol. 3, published by Shujunsha). Specifically, pCES30 was digested with BamHI (manufactured by Takara Shuzo), subjected to an agarose gel electrophoresis, and extracted and purified using GENECLEAN Kit (manufactured by BIO 101). The both ends of the resulting pCES30 fragment were blunted with DNA Blunting Kit (manufactured by Takara Shuzo) according to the attached protocol. The blunt-ended pCES30 fragment was concentrated by extraction with phenol/chloroform and precipitation with ethanol, and allowed

to react in the presence of Taq polymerase (manufactured by Roche Diagnostics) and dTTP at 70°C for 2 hours so that a nucleotide, thymine (T), was added to the 3'-end to prepare a T vector of pCES30.

[0378] Separately, chromosomal DNA was prepared from the lysine-producing B-6 strain according to the method of Saito et al. (*Biochem. Biophys. Acta, 72*: 619 (1963)). Using the chromosomal DNA as a template, PCR was carried out with Pfu turbo DNA polymelase (manufactured by Stratagene). In the mutated *hom* gene, the DNAs having the nucleotide sequences represented by SEQ ID NOS:7002 and 7003 were used as the primer set. In the mutated *pyc* gene, the DNAs having the nucleotide sequences represented by SEQ ID NOS:7004 and 7005 were used as the primer set. The resulting PCR product was subjected to agarose gel electrophoresis, and extracted and purified using GENE-GLEAN Kit (manufactured by BIO 101). Then, the PCR product was allowed to react in the presence of Taq polymerase (manufactured by Roche Diagnostics) and dATP at 72°C for 10 minutes so that a nucleotide, adenine (A), was added to the 3'-end.

10

15

25

30

35

40

45

[0379] The above pCES30 T vector fragment and the mutated *hom* gene (1.7 kb) or mutated *pyc* gene (3.6 kb) to which the nucleotide A had been added of the PCR product were concentrated by extraction with phenol/chloroform and precipitation with ethanol, and then ligated using Ligation Kit ver. 2. The ligation products were introduced into the ATCC 13032 strain according to the electroporation method, and cultured on BYG agar medium containing 25 µg/ml kanamycin at 30°C for 2 days to obtain kanamycin-resistant transformants. Each of the resulting transformants was cultured overnight in BYG liquid medium containing 25 µg/ml kanamycin, and a plasmid was extracted from the culturing solution medium according to the alkali SDS method. As a result of digestion analysis using restriction enzymes, it was confirmed that the plasmid had a structure in which the 1.7 kb or 3.6 kb DNA fragment had been inserted into pCES30. The plasmids thus constructed were named respectively pChom59 and pCpyc458.

[0380] The introduction of the mutations to the wild type ATCC 13032 strain and the lysine-producing No. 58 strain according to the gene replacement method was carried out according to the following method. Specifically, pChom59 and pCpyc458 were introduced to the ATCC 13032 strain and the No. 58 strain, respectively, and strains in which the plasmid is integrated into the chromosomal DNA by homologous recombination were selected using the method of lkeda et al. (Microbiology 144: 1863 (1998)). Then, the stains in which the second homologous recombination was carried out were selected by a selection method, making use of the fact that the Bacillus subtilis levansucrase encoded by pCES30 produced a suicidal substance (J. of Bacteriol., 174: 5462 (1992)). Among the selected strains, strains in which the wild type hom and pyc genes possessed by the ATCC 13032 strain and the No. 58 strain were replaced with the mutated hom and pyc genes, respectively, were isolated. The method is specifically explained below.

[0381] One strain was selected from the transformants containing the plasmid, pChom59 or pCpyc458, and the selected strain was cultured in BYG medium containing 20 μg/ml kanamycin, and pCG11 (Japanese Published Examined Patent Application No. 91827/94) was introduced thereinto by the electroporation method. pCG11 is a plasmid vector having a spectinomycin-resistant gene and a replication origin which is the same as pCE53. After introduction of the pCGII, the strain was cultured on BYG agar medium containing 20 μg/ml kanamycin and 100 μg/ml spectinomycin at 30°C for 2 days to obtain both the kanamycin- and spectinomycin-resistant transformant. The chromosome of one strain of these transformants was examined by the Southern blotting hybridization according to the method reported by Ikeda *et al.* (*Microbiology, 144*: 1863 (1998)). As a result, it was confirmed that pChom59 or pCpyc458 had been integrated into the chromosome by the homologous recombination of the Cambell type. In such a strain, the wild type and mutated *hom* or *pyc* genes are present closely on the chromosome, and the second homologous recombination is liable to arise therebetween.

[0382] Each of these transformants (having been recombined once) was spread on Suc agar medium (medium prepared by adding 100 g of sucrose, 7 g of meat extract, 10 g of peptone, 3 g of sodium chloride, 5 g of yeast extract (manufactured by Difco), and 18 g of Bactoagar (manufactured by Difco) to 1 liter of water, and adjusting its pH 7.2) and cultured at 30°C for a day. Then the colonies thus growing were selected in each case. Since a strain in which the sacB gene is present converts sucrose into a suicide substrate, it cannot grow in this medium (J. Bacteriol., 174: 5462 (1992)). On the other hand, a strain in which the sacB gene was deleted due to the second homologous recombination between the wild type and the mutated hom or pyc genes positioned closely to each other forms no suicide substrate and, therefore, can grow in this medium. In the homologous recombination, either the wild type gene or the mutated gene is deleted together with the sacB gene. When the wild type is deleted together with the sacB gene, the gene replacement into the mutated type arises.

[0383] Chromosomal DNA of each the thus obtained second recombinants was prepared by the above method of Saito *et al.* PCR was carried out using Pfu turbo DNA polymerase (manufactured by Stratagene) and the attached buffer. In the *hom* gene, DNAs having the nucleotide sequences represented by SEQ ID NOS:7002 and 7003 were used as the primer set. Also, in the *pyc* gene was used, DNAs having the nucleotide sequences represented by SEQ ID NOS:7004 and 7005 were used as the primer set. The nucleotide sequences of the PCR products were determined by the conventional method so that it was judged whether the *hom* or *pyc* gene of the second recombinant was a wild type or a mutant. As a result, the second recombinant which were called HD-1 and No. 58pyc were target strains having the mutated *hom* gene and *pyc* gene, respectively.

(3) Lysine production test of HD-1 and No. 58pyc strains

[0384] The HD-1 strain (strain obtained by incorporating the mutation, Val59Ala, in the *hom* gene into the ATCC 13032 strain) and the No. 58pyc strain (strain obtained by incorporating the mutation, Pro458Ser, in the *pyc* gene into the lysine-producing No. 58 strain) were subjected to a culture test in a 5 l jar fermenter by using the ATCC 13032 strain and the lysine-producing No. 58 strain respectively as a control. Thus lysine production was examined.

[0385] After culturing on BYG agar medium at 30°C for 24 hours, each strain was inoculated into 250 ml of a s ed medium (medium prepared by adding 50 g of sucrose, 40 g of corn steep liquor, 8.3 g of ammonium sulfate, 1 g of urea, 2 g of potassium dihydrogenphosphate, 0.83 g of magnesium sulfate heptahydrate, 10 mg of iron sulfate heptahydrate, 1 mg of copper sulfate pentahydrate, 10 mg of zinc sulfate heptahydrate, 10 mg of  $\beta$ -alanine, 5 mg of nicotinic acid, 1.5 mg of thiamin hydrochloride, and 0.5 mg of biotin to 1 liter of water, and adjusting its pH to 7.2, then to which 30 g of calcium carbonate had been added) contained in a 2 1 buffle-attached Erlenmeyer flask and cultured therein at 30°C for 12 to 16 hours. A total amount of the seed culturing medium was inoculated into 1,400 ml of a main culture medium (medium prepared by adding 60 g of glucose, 20 g of corn steep liquor, 25 g of ammonium chloride, 2.5 g of potassium dihydrogenphosphate, 0.75 g of magnesium sulfate heptahydrate, 50 mg of iron sulfate heptahydrate, 13 mg of manganese sulfate pentahydrate, 50 mg of calcium chloride, 6.3 mg of copper sulfate pentahydrate, 1.3 mg of zinc sulfate heptahydrate, 5 mg of nickel chloride hexahydrate, 1.3 mg of cobalt chloride hexahydrate, 1.3 mg of ammonium molybdenate tetrahydrate, 14 mg of nicotinic acid, 23 mg of β-alanine, 7 mg of thiamin hydrochloride, and 0.42 mg of biotin to 1 liter of water) contained in a 5 1 jar fermenter and cultured therein at 32°C, 1 vvm and 800 rpm while controlling the pH to 7.0 with aqueous ammonia. When glucose in the medium had been consumed, a glucose feeding solution (medium prepared by adding 400 g glucose and 45 g of ammonium chloride to 1 liter of water) was continuously added. The addition of feeding solution was carried out at a controlled speed so as to maintain the dissolved oxygen concentration within a range of 0.5 to 3 ppm. After culturing for 29 hours, the culture was terminated. The cells were separated from the culture medium by centrifugation and then L-lysine hydrochloride in the supernatant was quantified by high performance liquid chromatography (HPLC). The results are shown in Table 2 below.

Table 2

Strain	L-Lysine hydrochloride yield (g/l)
ATCC 13032	0
HD-1	8
No. 58	45
No. 58pyc	51

[0386] As is apparent from the results shown in Table 2, the lysine productivity was improved by introducing the mutation, Val59Ala, in the *hom* gene or the mutation, Pro458Ser, in the pyc gene. Accordingly, it was found that the mutations are both effective mutations relating to the production of lysine. Strain, AHP-3, in which the mutation, Val59Ala, in the *hom* gene and the mutation, Pro458Ser, in the *pyc* gene have been introduced into the wild type ATCC 13032 strain together with the mutation, Thr331lle in the *lysC* gene has been deposited on December 5, 2000, in National Institute of Bioscience and Human Technology, Agency of Industrial Science and Technology (Higashi 1-1-3, Tsukuba-shi, Ibaraki, Japan) as FERM BP-7382.

## Example 3

10

15

20

25

30

35

40

45

55

Reconstruction of lysine-producing strain based on genome information

[0387] The lysine-producing mutant B-6 strain (*Appl. Microbiol. Biotechnol., 32*: 269-273 (1989)), which has been constructed by multiple round random mutagenesis with NTG and screening from the wild type ATCC 13032 strain, produces a remarkably large amount of lysine hydrochloride when cultured in a jar at 32°C using glucose as a carbon source. However, since the fermentation period is long, the production rate is less than 2.1 g/l/h. Breeding to reconstitute only effective mutations relating to the production of lysine among the estimated at least 300 mutations introduced into the B-6 strain in the wild type ATCC 13032 strain was performed.

(1) Identification of mutation point and effective mutation by comparing the gene nucleotide sequence of the B-6 strain with that of the ATCC 13032 strain

[0388] As described above, the nucleotide sequences of genes derived from the B-6 strain were compared with the

corresponding nucleotide sequences of the ATCC 13032 strain genome represented by SEQ ID NOS:1 to 3501 and analyzed to identify many mutation points accumulated in the chromosome of the B-6 strain. Among these, a mutation, Val591Ala, in hom, a mutation, Thr311lle, in lysC, a mutation, Pro458Ser, in pyc and a mutation, Ala213Thr, in zwf were specified as effective mutations relating to the production of lysine. Breeding to reconstitute the 4 mutations in the wild type strain and for constructing of an industrially important lysine-producing strain was carried out according to the method shown below.

(2) Construction of plasmid for gene replacement having mutated gen

5

10

25

30

35

40

45

[0389] The plasmid for gene replacement, pChom59, having the mutated *hom* gene and the plasmid for gene replacement, pCpyc458, having the mutated *pyc* gene were prepared in the above Example 2(2). Plasmids for gene replacement having the mutated *lysC* and *zwf* were produced as described below.

[0390] The *lysC* and *zwf* having mutation points were amplified by PCR, and inserted into a plasmid for gene replacement, pCES30, according to the TA cloning method described in Example 2(2) (Bio Experiment Illustrated, Vol. 3). [0391] Separately, chromosomal DNA was prepared from the lysine-producing B-6 strain according to the above method of Saito *et al.* Using the chromosomal DNA as a template, PCR was carried out with Pfu turbo DNA polymerase (manufactured by Stratagene). In the mutated *lysC* gene, the DNAs having the nucleotide sequences represented by SEQ ID NOS:7006 and 7007 were used as the primer set. In the mutated *zwf* gene, the DNAs having the nucleotide sequences represented by SEQ ID NOS:7008 and 7009 as the primer set. The resulting PCR product was subjected to agarose gel electrophoresis, and extracted and purified using GENEGLEAN Kit (manufactured by BIO 101). Then, the PCR product was allowed to react in the presence of Taq DNA polymerase (manufactured by Roche Diagnostics) and dATP at 72°C for 10 minutes so that a nucleotide, adenine (A), was added to the 3'-end.

[0392] The above pCES30 T vector fragment and the mutated *lysC* gene (1.5 kb) or mutated *zwf* gene (2.3 kb) to which the nucleotide A had been added of the PCR product were concentrated by extraction with phenol/chloroform and precipitation with ethanol, and then ligated using Ligation Kit ver. 2. The ligation products were introduced into the ATCC 13032 strain according to the electroporation method, and cultured on BYG agar medium containing 25 μg/ml kanamycin at 30°C for 2 days to obtain kanamycin-resistant transformants. Each of the resulting transformants was cultured overnight in BYG liquid medium containing 25 μg/ml kanamycin, and a plasmid was extracted from the culturing solution medium according to the alkali SDS method. As a result of digestion analysis using restriction enzymes, it was confirmed that the plasmid had a structure in which the 1.5 kb or 2.3 kb DNA fragment had been inserted into pCES30. The plasmids thus constructed were named respectively pClysC311 and pCzwf213.

(3) Introduction of mutation, Thr311lle, in IysC into one point mutant HD-1

[0393] Since the one mutation point mutant HD-1 in which the mutation, Val59Ala, in *hom* was introduced into the wild type ATCC 13032 strain had been obtained in Example 2(2), the mutation, Thr311lle, in *lysC* was introduced into the HD-1 strain using pClysC311 produced in the above (2) according to the gene replacement method described in Example 2(2). PCR was carried out using chromosomal DNA of the resulting strain and, as the primer set, DNAs having the nucleotide sequences represented by SEQ ID NOS:7006 and 7007 in the same manner as in Example 2(2). As a result of the fact that the nucleotide sequence of the PCR product was determined in the usual manner, it was confirmed that the strain which was named AHD-2 was a two point mutant having the mutated *lysC* gene in addition to the mutated *hom* gene.

(4) Introduction of mutation, Pro458Ser, in pyc into two point mutant AHD-2

[0394] The mutation, Pro458Ser, in *pyc* was introduced into the AHD-2 strain using the pCpyc458 produced in Example 2(2) by the gene replacement method described in Example 2(2). PCR was carried out using chromosomal DNA of the resulting strain and, as the primer set, DNAs having the nucleotide sequences represented by SEQ ID NOS:7004 and 7005 in the same manner as in Example 2(2). As a result of the fact that the nucleotide sequence of the PCR product was determined in the usual manner, it was confirmed that the strain which was named AHD-3 was a three point mutant having the mutated *pyc* gene in addition to the mutated *hom* gene and *lysC* gene.

(5) Introduction of mutation, Ala213Thr, in zwf into three point mutant AHP-3

[0395] The mutation, Ala213Thr, in zwf was introduced into the AHP-3 strain using the pCzwf458 produced in the above (2) by the gene replacement method described in Example 2(2). PCR was carried out using chromosomal DNA of the resulting strain and, as the primer set, DNAs having the nucleotide sequences represented by SEQ ID NOS: 7008 and 7009 in the same manner as in Example 2(2). As a result of the fact that the nucleotide sequence of the PCR

product was determined in the usual manner, it was confirmed that the strain which was named APZ-4 was a four point mutant having the mutated *zwf* gene in addition to the mutated *hom* gene, *lysC* gene and *pyc* gene.

(6) Lysine production test on HD-1, AHD-2, AHP-3 and APZ-4 strains

[0396] The HD-1, AHD-2, AHP-3 and APZ-4 strains obtained above were subjected to a culture test in a 5 I jar fermenter in accordance with the method of Example 2(3).

[0397] Table 3 shows the results.

5

10

15

20

25

30

35

40

45

50

Table 3

Strain	L-Lysine hydrochloride (g/l)	Productivity (g/l/h)
HD-1	8	0.3
AHD-2	73	2.5
AHP-3	80	2.8
APZ-4	86	3.0

[0398] Since the lysine-producing mutant B-6 strain which has been bred based on the random mutation and selection shows a productivity of less than 2.1 g/l/h, the APZ-4 strain showing a high productivity of 3.0 g/l/h is useful in industry.

(7) Lysine fermentation by APZ-4 strain at high temperature

[0399] The APZ-4 strain, which had been reconstructed by introducing 4 effective mutations into the wild type strain, was subjected to the culturing test in a 5 l jar fermenter in the same manner as in Example 2(3), except that the culturing temperature was changed to 40°C.

[0400] The results are shown in Table 4.

Table 4

Temper	ature (°C)	L-Lysine hydrochloride (g/l)	Productivity (g/l/h)
1	32	86	3.0
	40	95	3.3

[0401] As is apparent from the results shown in Table 4, the lysine hydrochloride titer and productivity in culturing at a high temperature of 40°C comparable to those at 32°C were obtained. In the mutated and bred lysine-producing B-6 strain constructed by repeating random mutation and selection, the growth and the lysine productivity are lowered at temperatures exceeding 34°C so that lysine fermentation cannot be carried out, whereas lysine fermentation can be carried out using the APZ-4 strain at a high temperature of 40°C so that the load of cooling is greatly reduced and it is industrially useful. The lysine fermentation at high temperatures can be achieved by reflecting the high temperature adaptability inherently possessed by the wild type strain on the APZ-4 strain.

[0402] As demonstrated in the reconstruction of the lysine-producing strain, the present invention provides a novel breeding method effective for eliminating the problems in the conventional mutants and acquiring industrially advantageous strains. This methodology which reconstitutes the production strain by reconstituting the effective mutation is an approach which is efficiently carried out using the nucleotide sequence information of the genome disclosed in the present invention, and its effectiveness was found for the first time in the present invention.

### Example 4

Production of DNA microarray and use thereof

[0403] A DNA microarray was produced based on the nucleotide sequence information of the ORF deduced from the full nucleotide sequences of *Corynebacterium glutamicum* ATCC 13032 using software, and genes of which expression is fluctuated depending on the carbon source during culturing were searched.

(1) Production of DNA microarray

[0404] Chromosomal DNA was prepared from Corynebacterium glutamicum ATCC 13032 by the method of Saito et

al. (Biochem. Biophys. Acta, 72: 619 (1963)). Based on 24 genes having the nucleotide sequences represented by SEQ ID NOS:207, 3433, 281, 3435, 3439, 765, 3445, 1226, 1229, 3448, 3451, 3453, 3455, 1743, 3470, 2132, 3476, 3477, 3485, 3488, 3489, 3494, 3496, and 3497 from the ORFs shown in Table 1 deduced from the full genome nucleotide sequence of Corynebacterium glutamicum ATCC 13032 using software and the nucleotide sequence of rabbit globin gene (GenBank Accession No. V00882) used as an internal standard, oligo DNA primers for PCR amplification represented by SEQ ID NOS:7010 to 7059 targeting the nucleotide sequences of the genes were synthesized in a usual manner.

[0405] As the oligo DNA primers used for the PCR,

15

25

30

40

45

[0406] DNAs having the nucleotide sequence represented by SEQ ID NOS:7010 and 7011 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:207.

[0407] DNAs having the nucleotide sequence represented by SEQ ID NOS:7012 and 7013 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3433.

[0408] DNAs having the nucleotide sequence represented by SEQ ID NOS:7014 and 7015 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:281,

[0409] DNAs having the nucleotide sequence represented by SEQ ID NOS:7016 and 7017 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3435,

[0410] DNAs having the nucleotide sequence represented by SEQ ID NOS:7018 and 7019 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3439.

[0411] DNAs having the nucleotide sequence represented by SEQ ID NOS:7020 and 7021 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:765,

[0412] DNAs having the nucleotide sequence represented by SEQ ID NOS:7022 and 7023 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3445,

[0413] DNAs having the nucleotide sequence represented by SEQ ID NOS:7024 and 7025 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:1226,

[0414] DNAs having the nucleotide sequence represented by SEQ ID NOS:7026 and 7027 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:1229,

[0415] DNAs having the nucleotide sequence represented by SEQ ID NOS:7028 and 7029 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3448,

[0416] DNAs having the nucleotide sequence represented by SEQ ID NOS:7030 and 7031 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3451,

[0417] DNAs having the nucleotide sequence represented by SEQ ID NOS:7032 and 7033 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3453,

[0418] DNAs having the nucleotide sequence represented by SEQ ID NOS:7034 and 7035 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3455,

[0419] DNAs having the nucleotide sequence represented by SEQ ID NOS:7036 and 7037 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:1743,

[0420] DNAs having the nucleotide sequence represented by SEQ ID NOS:7038 and 7039 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3470,

[0421] DNAs having the nucleotide sequence represented by SEQ ID NOS:7040 and 7041 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:2132,

[0422] DNAs having the nucleotide sequence represented by SEQ ID NOS:7042 and 7043 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3476,

[0423] DNAs having the nucleotide sequence represented by SEQ ID NOS:7044 and 7045 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3477,

[0424] DNAs having the nucleotide sequence represented by SEQ ID NOS:7046 and 7047 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3485,

[0425] DNAs having the nucleotide sequence represented by SEQ ID NOS:7048 and 7049 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3488,

[0426] DNAs having the nucleotide sequence represented by SEQ ID NOS:7050 and 7051 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3489,

[0427] DNAs having the nucleotide sequence represented by SEQ ID NOS:7052 and 7053 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3494,

[0428] DNAs having the nucleotide sequence represented by SEQ ID NOS:7054 and 7055 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3496,

[0429] DNAs having the nucleotide sequence represented by SEQ ID NOS:7056 and 7057 were used for the amplification of the DNA having the nucleotide sequence represented by SEQ ID NO:3497, and

[0430] DNAs having the nucleotide sequence represented by SEQ ID NOS:7058 and 7059 were used for the amplification of the DNA having the nucleotide sequence of the rabbit globin gene,

as the respective primer set.

[0431] The PCR was carried for 30 cycles with each cycle consisting of 15 seconds at 95°C and 3 minutes at 68°C using a thermal cycler (GeneAmp PCR system 9600, manufactured by Perkin Elmer), TaKaRa EX-Taq (manufactured by Takara Shuzo), 100 ng of the chromosomal DNA and the buffer attached to the TaKaRa Ex-Taq reagent. In the case of the rabbit globin gene, a single-stranded cDNA which had been synthesized from rabbit globin mRNA (manufactured by Life Technologies) according to the manufacture's instructions using a reverse transcriptase RAV-2 (manufactured by Takara Shuzo). The PCR product of each gene thus amplified was subjected to agarose gel electrophoresis and extracted and purifi d using QIAquick Gel Extraction Kit (manufactured by QIAGEN). The purified PCR product was concentrated by precipitating it with ethanol and adjusted to a concentration of 200 ng/µl. Each PCR product was spotted on a slide glass plate (manufactured by Matsunami Glass) having MAS coating in 2 runs using GTMASS SYSTEM (manufactured by Nippon Laser & Electronics Lab.) according to the manufacture's instructions.

## (2) Synthesis of fluorescence labeled cDNA

10

15

20

30

35

40

45

50

55

[0432] The ATCC 13032 strain was spread on BY agar medium (medium prepared by adding 20 g of peptone (manufactured by Kyokuto Pharmaceutical), 5 g of yeast extract (manufactured by Difco), and 16 g of Bactoagar (manufactured by Difco) to in 1 liter of water and adjusting its pH to 7.2) and cultured at 30°C for 2 days. Then, the cultured strain was further inoculated into 5 ml of BY liquid medium and cultured at 30°C overnight. Then, the cultured strain was further inoculated into 30 ml of a minimum medium (medium prepared by adding 5 g of ammonium sulfate, 5 g of urea, 0.5 g of monopotassium dihydrogenphosphate, 0.5 g of dipotassium monohydrogenphosphate, 20.9 g of morpholinopropanesulfonic acid, 0.25 g of magnesium sulfate heptahydrate, 10 mg of calcium chloride dihydrate, 10 mg of manganese sulfate monohydrate, 10 mg of ferrous sulfate heptahydrate, 1 mg of zinc sulfate heptahydrate, 0.2 mg copper sulfate, and 0.2 mg biotin to 1 liter of water, and adjusting its pH to 6.5) containing 110 mmol/l glucose or 200 mmol/I ammonium acetate, and cultured in an Erlenmyer flask at 30° to give 1.0 of absorbance at 660 nm. After the cells were prepared by centrifuging at 4°C and 5,000 rpm for 10 minutes, total RNA was prepared from the resulting cells according to the method of Bormann et al. ( Molecular Microbiology, 6: 317-326 (1992)). To avoid contamination with DNA, the RNA was treated with Dnasel (manufactured by Takara Shuzo) at 37°C for 30 minutes and then further purified using Qiagen RNeasy MiniKit (manufactured by QIAGEN) according to the manufacture's instructions. To 30 µg of the resulting total RNA, 0.6 µl of rabbit globin mRNA (50 ng/µl, manufactured by Life Technologies) and 1 µl of a random 6 mer primer (500 ng/μl, manufactured by Takara Shuzo) were added for denaturing at 65°C for 10 minutes, followed by guenching on ice. To the resulting solution, 6 µl of a buffer attached to Superscript II (manufactured by Lifetechnologies), 3 μl of 0.1 mol/l DTT, 1.5 μl of dNTPs (25 mmol/l dATP, 25 mmol/l dCTP, 25 mmol/l dGTP, 10 mmol/ IdTTP), 1.5 µl of Cv5-dUTP or Cv3-dUTP (manufactured by NEN) and 2 µl of Superscript II were added, and allowed to stand at 25°C for 10 minutes and then at 42°C for 110 minutes. The RNA extracted from the cells using glucose as the carbon source and the RNA extracted from the cells using ammonium acetate were labeled with Cy5-dUTP and Cy3-dUTP, respectively. After the fluorescence labeling reaction, the RNA was digested by adding 1.5 μl of 1 mol/l sodium hydroxide-20 mmol/l EDTA solution and 3.0 µl of 10% SDS solution, and allowed to stand at 65°C for 10 minutes. The two cDNA solutions after the labeling were mixed and purified using Qiagen PCR purification Kit (manufactured by QIAGEN) according to the manufacture's instructions to give a volume of 10 µl.

# (3) Hybridization

[0433] UltraHyb (110 µl) (manufactured by Ambion) and the fluorescence-labeled cDNA solution (10 µl) were mixed and subjected to hybridization and the subsequent washing of slide glass using GeneTAC Hybridization Station (manufactured by Genomic Solutions) according to the manufacture's instructions. The hybridization was carried out at 50°C, and the washing was carried out at 25°C.

#### (4) Fluorescence analysis

[0434] The fluorescence amount of each DNA array having the fluorescent cDNA hybridized therewith was measured using ScanArray 4000 (manufactured by GSI Lumonics).

[0435] Table 5 shows the Cy3 and Cy5 signal intensities of the genes having been corrected on the basis of the data of the rabbit globin used as the internal standard and the Cy3/Cy5 ratios.

Table	5
-------	---

SEQ ID NO	Cy3 intensity	Cy5 intensity	Cy3/Cy5
207	5248	3240	1.62

Table 5 (continued)

(667,111,1263)				
SEQ ID NO	Cy3 intensity	Cy5 intensity	Cy3/Cy5	
3433	2239	2694	0.83	
281	2370	2595	0.91	
3435	2566	2515	1.02	
3439	5597	6944	0.81	
765	6134	4943	1.24	
3455	1169	1284	0.91	
1226	1301	1493	0.87	
1229	1168	1131	1.03	
3448	1187	1594	0.74	
3451	2845	3859	0.74	
3453	3498	1705	2.05	
3455	1491	1144	1.30	
1743	1972	1841	1.07	
3470	4752	3764	1.26	
2132	1173	1085	1.08	
3476	1847	1420	1.30	
3477	1284	1164	1.10	
3485	4539	8014	0.57	
3488	34289	1398	24.52	
3489	43645	1497	29.16	
3494	3199	2503	1.28	
3496	3428	2364	1.45	
3497	3848	3358	.1.15	

[0436] The ORF function data estimated by using software were searched for SEQ ID NOS:3488 and 3489 showing remarkably strong Cy3 signals. As a result, it was found that SEQ ID NOS:3488 and 3489 are a maleate synthase gene and an isocitrate lyase gene, respectively. It is known that these genes are transcriptionally induced by acetic acid in *Corynebacterium glutamicum* (*Archives of Microbiology, 168*: 262-269 (1997)).

[0437] As described above, a gene of which expression is fluctuates could be discovered by synthesizing appropriate oligo DNA primers based on the ORF nucleotide sequence information deduced from the full genomic nucleotide sequence information of *Corynebacterium glutamicum* ATCC 13032 using software, amplifying the nucleotide sequences of the gene using the genome DNA of *Corynebacterium glutamicum* as a template in the PCR reaction, and thus producing and using a DNA microarray.

[0438] This Example shows that the expression amount can be analyzed using a DNA microarray in the 24 genes. On the other hand, the present DNA microarray techniques make it possible to prepare DNA microarrays having thereon several thousand gene probes at once. Accordingly, it is also possible to prepare DNA microarrays having thereon all of the ORF gene probes deduced from the full genomic nucleotide sequence of *Corynebacterium glutamicum* ATCC 13032 determined by the present invention, and analyze the expression profile at the total gene level of *Corynebacterium glutamicum* using these arrays.

### Example 5

10

15

20

25

30

35

45

50

55

Homology search using Corynebacterium glutamicum genome sequence

## (1) Search of adenosine deaminase

[0439] The amino acid sequence (ADD\_ECOLI) of *Escherichia coli* adenosine deaminase was obtained from Swiss-prot Database as the amino acid sequence of the protein of which function had been confirmed as adenosine deaminase (EC3.5.4.4). By using the full length of this amino acid sequence as a query, a homology search was carried out on a nucleotide sequence database of the genome sequence of *Corynebacterium glutamicum* or a database of the amino acids in the ORF region deduced from the genome sequence using FASTA program (*Proc. Natl. Acad. Sci. ISA, 85*: 2444-2448 (1988)). A case where E-value was le-10 or 1 ss was judged as being significantly homologous. As a result,

no sequence significantly homologous with the *Escherichia coli* adenosine deaminase was found in the nucleotide sequence database of the genome sequence of *Corynebacterium glutamicum* or the database of the amino acid sequences in the ORF region deduced from the genome sequence. Based on these results, it is assumed that *Corynebacterium glutamicum* contains no ORF having adenosine deaminase activity and thus has no activity of converting adenosine into inosine.

## (2) Search of glycine cleavage enzyme

5

10

15

20

25

30

35

45

50

55

**[0440]** The sequences (GCSP\_ECOLI, GCST\_ECOLI and GCSH\_ECOLI) of glycine decarboxylase, aminomethyl transferase and an aminomethyl group carrier each of which is a component of *Escherichia coli* glycine cleavage enzyme as the amino acid sequence of the protein, of which function had been confirmed as glycine cleavage enzyme (EC2.1.2.10), were obtained from Swiss-prot Database.

[0441] By using these full-length amino acid sequences as a query, a homology search was carried out on a nucleotide sequence database of the genome sequence of *Corynebacterium glutamicum* or a database of the ORF amino acid sequences deduced from the genome sequence using FASTA program. A case where E-value was le-10 or less was judged as being significantly homologous. As a result, no sequence significantly homologous with the glycine decarboxylase, the aminomethyl transferase or the aminomethyl group carrier each of which is a component of *Escherichia coli* glycine cleavage enzyme, was found in the nucleotide sequence database of the genome sequence of *Corynebacterium glutamicum* or the database of the ORF amino acid sequences estimated from the genome sequence. Based on these results, it is assumed that *Corynebacterium glutamicum* contains no ORF having the activity of glycine decarboxylase, aminomethyl transferase or the aminomethyl group carrier and thus has no activity of the glycine cleavage enzyme.

## (3) Search of IMP dehydrogenase

[0442] The amino acid sequence (IMDH ECOLI) of Escherichia coli IMP dehydrogenase as the amino acid sequence of the protein, of which function had been confirmed as IMP dehydrogenase (EC1.1.1.205), was obtained from Swissprot Database. By using the full length of this amino acid sequence as a query, a homology search was carried out on a nucleotide sequence database of the genome sequence of Corynebacterium glutamicum or a database of the ORF amino acid sequences predicted from the genome sequence using FASTA program. A case where E-value was le-10 or less was judged as being significantly homologous. As a result, the amino acid sequences encoded by two ORFs. namely, an ORF positioned in the region of the nucleotide sequence No. 615336 to 616853 (or ORF having the nucleotide sequence represented by SEQ ID NO:672) and another ORF positioned in the region of the nucleotide sequence No. 616973 to 618094 (or ORF having the nucleotide sequence represented by SEQ ID NO:674) were significantly homologous with the ORFs of Escherichia coli IMP dehydrogenase. By using the above-described predicted amino acid sequence as a query in order to examine the similarity of the amino acid sequences encoded by the ORFs with IMP dehydrogenases of other organisms in greater detail, a search was carried out on GenBank (http://www.ncbi.nlm. nih.gov/) nr-aa database (amino acid sequence database constructed on the basis of GenBankCDS translation products, PDB database, Swiss-Prot database, PIR database, PRF database by eliminating duplicated registrations) using BLAST program. As a result, both of the two amino acid sequences showed significant homologies with IMP dehdyrogenases of other organisms and clearly higher homologies with IMP dehdyrogenases than with amino acid sequences of other proteins, and thus, it was assumed that the two ORFs would function as IMP dehydrogenase. Based on these results, it was therefore assumed that Corynebacterium glutamicum has two ORFs having the IMP dehydrogenase activity.

# Example 6

Proteome analysis of proteins derived from Corynebacterium glutamicum

(1) Preparations of proteins derived from *Corynebacterium glutamicum* ATCC 13032, FERM BP-7134 and FERM BP-158

[0443] Culturing tests of *Corynebacterium glutamicum* ATCC 13032 (wild type strain), *Corynebacterium glutamicum* FERM BP-7134 (lysine-producing strain) and *Corynebacterium glutamicum* (FERM BP-158, lysine-highly producing strain) were carried out in a 51 jar fermenter according to the method in Example 2(3). The results are shown in Table 6.

Table 6

Strain	L-Lysine yield (g/l)
ATCC 13032	0
FERM BP-7134	45
FERM BP-158	60

[0444] After culturing, cells of each strain were recovered by centrifugation. These cells were washed with Tris-HCl buffer (10 mmol/l Tris-HCl, pH 6.5, 1.6 mg/ml protease inhibitor (COMPLETE; manufactured by Boehringer Mannheim)) three times to give washed cells which could be stored under freezing at -80°C. The freeze-stored cells were thawed before use, and used as washed cells.

[0445] The washed cells described above were suspended in a disruption buffer (10 mmol/l Tris-HCl, pH 7.4, 5 mmol/l magnesium chloride, 50 mg/l RNase, 1.6 mg/ml protease inhibitor (COMPLETE: manufactured by Boehringer Mannheim)), and disrupted with a disruptor (manufactured by Brown) under cooling. To the resulting disruption solution, DNase was added to give a concentration of 50 mg/l, and allowed to stand on ice for 10 minutes. The solution was centrifuged (5,000  $\times$  g, 15 minutes, 4°C) to remove the undisrupted cells as the precipitate, and the supernatant was recovered.

[0446] To the supernatant, urea was added to give a concentration of 9 mol/l, and an equivalent amount of a lysis buffer (9.5 mol/l urea, 2% NP-40, 2% Ampholine, 5% mercaptoethanol, 1.6 mg/ml protease inhibitor (COMPLETE; manufactured by Boehringer Mannheim) was added thereto, followed by thoroughly stirring at room temperature for dissolving.

[0447] After being dissolved, the solution was centrifuged at  $12,000 \times g$  for 15 minutes, and the supernatant was recovered.

[0448] To the supernatant, ammonium sulfate was added to the extent of 80% saturation, followed by thoroughly stirring for dissolving.

**[0449]** After being dissolved, the solution was centrifuged (16,000  $\times$  g, 20 minutes, 4°C), and the precipitate was recovered. This precipitate was dissolved in the lysis buffer again and used in the subsequent procedures as a protein sample. The protein concentration of this sample was determined by the method for quantifying protein of Bradford.

(2) Separation of protein by two dimensional electrophoresis

10

15

20

25

30

35

45

55

[0450] The first dimensional electrophoresis was carried out as described below by the isoelectric electrophoresis method.

[0451] A molded dry IPG strip gel (pH 4-7, 13 cm, Immobiline DryStrips; manufactured by Amersham Pharmacia Biotech) was set in an electrophoretic apparatus (Multiphor II or IPGphor; manufactured by Amersham Pharmacia Biotech) and a swelling solution (8 mol/l urea, 0.5% Triton X-100, 0.6% dithiothreitol, 0.5% Ampholine, pH 3-10) was packed therein, and the gel was allowed to stand for swelling 12 to 16 hours.

[0452] The protein sample prepared above was dissolved in a sample solution (9 mol/l urea, 2% CHAPS, 1% dithiothreitol, 2% Ampholine, pH 3-10), and then about 100 to 500 μg (in terms of protein) portions thereof were taken and added to the swollen IPG strip gel.

[0453] The electrophoresis was carried out in the 4 steps as defined below under controlling the temperature to 20°C:

- step 1: 1 hour under a gradient mode of 0 to 500V;
- step 2: 1 hour under a gradient mode of 500 to 1,000 V;
- step 3: 4 hours under a gradient mode of 1,000 to 8,000 V; and
- step 4: 1 hour at a constant voltage of 8,000 V.

[0454] After the isoelectric electrophoresis, the IPG strip gel was put off from the holder and soaked in an equilibration buffer A (50 mmol/l Tris-HCl, pH 6.8, 30% glycerol, 1% SDS, 0.25% dithiothreitol) for 15 minutes and another equilibration buffer B (50 mmol/l Tris-HCl, pH 6.8, 6 mol/l urea, 30% glycerol, 1% SDS, 0.45% iodo acetamide) for 15 minutes to sufficiently equilibrate the gel.

[0455] After the equilibrium, the IPG strip gel was lightly rinsed in an SDS electrophoresis buffer (1.4% glycine, 0.1% SDS, 0.3% Tris-HCl, pH 8.5), and the second dimensional electrophoresis depending on molecular weight was carried out as described below to separate the proteins.

[0456] Specifically, the above IPG strip gel was closely placed on 14% polyacrylamide slub gel (14% polyacrylamide, 0.37% bisacrylamide, 37.5 mmol/l Tris-HCl, pH 8.8, 0.1% SDS, 0.1% TEMED, 0.1% ammonium persulfate) and sub-

jected to electrophoresis under a constant voltage of 30 mA at 20°C for 3 hours to separate the proteins.

(3) Detection of protein spot

10

15

20

25

40

45

- [0457] Coomassie staining was performed by the method of Gorg et al. (*Electrophoresis*, 9: 531-546 (1988)) for the slub gel after the second dimensional electrophoresis. Specifically, the slub gel was stained under shaking at 25°C for about 3 hours, the excessive coloration was removed with a decoloring solution, and the gel was thoroughly washed with distilled water.
  - [0458] The results are shown in Fig. 2. The proteins derived from the ATCC 13032 strain (Fig. 2A), FERM BP-7134 strain (Fig. 2B) and FERM BP-158 strain (Fig. 2C) could be separated and detected as spots.
  - (4) In-gel digestion of detected protein spot
  - [0459] The detected spots were each cut out from the gel and transferred into siliconized tube, and 400  $\mu$ l of 100 mmol/1 ammonium bicarbonate : acetonitrile solution (1:1, v/v) was added thereto, followed by shaking overnight and freeze-dried as such. To the dried gel, 10  $\mu$ l of a lysylendopeptidase (LysC) solution (manufactured by WAKO, prepared with 0.1% SDS-containing 50 mmol/l ammonium bicarbonate to give a concentration of 100 ng/ $\mu$ l) was added and the gel was allowed to stand for swelling at 0°C for 45 minutes, and then allowed to stand at 37°C for 16 hours. After removing the LysC solution, 20  $\mu$ l of an extracting solution (a mixture of 60% acetonitrile and 5% formic acid) was added, followed by ultrasonication at room temperature for 5 minutes to disrupt the gel. After the disruption, the extract was recovered by centrifugation (12,000 rpm, 5 minutes, room temperature). This operation was repeated twice to recover the whole extract. The recovered extract was concentrated by centrifugation *in vacuo* to halve the liquid volume. To the concentrate, 20  $\mu$ l of 0.1% trifluoroacetic acid was added, followed by thoroughly stirring, and the mixture was subjected to desalting using ZipTip (manufactured by Millipore). The protein absorbed on the carriers of ZipTip was eluted with 5  $\mu$ l of  $\alpha$ -cyano-4-hydroxycinnamic acid for use as a sample solution for analysis.
  - (5) Mass spectrometry and amino acid sequence analysis of protein spot with matrix assisted laser desorption ionization time of flight mass spectrometer (MALDI-TOFMS)
- 30 [0460] The sample solution for analysis was mixed in the equivalent amount with a solution of a peptide mixture for mass calibration (300 nmol/l Angiotensin II, 300 nmol/l Neurotensin, 150 nmol/l ACTHclip 18-39, 2.3 μmol/l bovine insulin B chain), and 1 μl of the obtained solution was spotted on a stainless probe and crystallized by spontaneously drying.
  - [0461] As measurement instruments, REFLEX MALDI-TOF mass spectrometer (manufactured by Bruker) and an N2 laser (337 nm) were used in combination.
  - [0462] The analysis by PMF (peptide-mass finger printing) was carried out using integration spectra data obtained by measuring 30 times at an accelerated voltage of 19.0 kV and a detector voltage of 1.50 kV under reflector mode conditions. Mass calibration was carried out by the internal standard method.
  - [0463] The PSD (post-source decay) analysis was carried out using integration spectra obtained by successively altering the reflection voltage and the detector voltage at an accelerated voltage of 27.5 kV.
  - [0464] The masses and amino acid sequences of the peptide fragments derived from the protein spot after digestion were thus determined.
  - (6) Identification of protein spot
  - [0465] From the amino acid sequence information of the digested peptide fragments derived from the protein spot obtained in the above (5), ORFs corresponding to the protein were searched on the genome sequence database of Corynebacterium glutamicum ATCC 13032 as constructed in Example 1 to identify the protein.
  - [0466] The identification of the protein was carried out using MS-Fit program and MS-Tag program of intranet protein prospector.
  - (a) Search and identification of gene encoding high-expression protein
- [0467] In the proteins derived from Corynebacterium glutamicum ATCC 13032 showing high expression amounts in CBB-staining shown in Fig. 2A, the proteins corresponding to Spots-1, 2, 3, 4 and 5 were identified by the above method. [0468] As a result, it was found that Spot-1 corresponded to enolase which was a protein having the amino acid sequence of SEQ ID NO:4585; Spot-2 corresponded to phosphoglycelate kinase which was a protein having the amino acid sequence of SEQ ID NO:5254; Spot-3 corresponded to glyceraldehyde-3-phosphate dehydrogenase which was

a protein having the amino acid sequence represented by SEQ ID NO:5255; Spot-4 corresponded to fructose bisphosphate aldolase which was a protein having the amino acid sequence represented by SEQ ID NO:6543; and Spot-5 corresponded to triose phosphate isomerase which was a protein having the amino acid sequence represented by SEQ ID NO:5252.

- [0469] These genes, represented by SEQ ID NOS:1085, 1754, 1775, 3043 and 1752 encoding the proteins corresponding to Spots-1, 2, 3, 4 and 5, respectively, encoding the known proteins are important in the central metabolic pathway for maintaining the life of the microorganism. Particularly, it is suggested that the genes of Spots-2, 3 and 5 form an operon and a high-expression promoter is encoded in the upstream thereof (*J. of Eacteriol., 174*: 6067-6086 (1992)).
  - [0470] Also, the protein corresponding to Spot-9 in Fig. 2 was identified in the same manner as described above, and it was found that Spot-9 was an elongation factor Tu which was a protein having the amino acid sequence represented by SEQ ID No:6937, and that the protein was encoded by DNA having the nucleotide sequence represented by SEQ ID No:3437.
  - [0471] Based on these results, the proteins having high expression level were identified by proteome analysis using the genome sequence database of *Corynebacterium glutamicum* constructed in Example 1. Thus, the nucleotide sequences of the genes encoding the proteins and the nucleotide sequences upstream thereof could be searched simultaneously. Accordingly, it is shown that nucleotide sequences having a function as a high-expression promoter can be efficiently selected.
  - (b) Search and identification of modified protein
    - [0472] Among the proteins derived from *Corynebacterium glutamicum* FERM BP-7134 shown in Fig. 2B, Spots-6, 7 and 8 were identified by the above method. As a result, these three spots all corresponded to catalase which was a protein having the amino acid sequence represented by SEQ ID NO:3785.
  - [0473] Accordingly, all of Spots-6, 7 and 8 detected as spots differing in isoelectric mobility were all products derived from a catalase gene having the nucleotide sequence represented by SEQ ID No:285. Accordingly, it is shown that the catalase derived from *Corynebacterium glutamicum* FERM BP-7134 was modified after the translation.
    - [0474] Based on these results, it is confirmed that various modified proteins can be efficiently searched by proteome analysis using the genome sequence database of *Corynebacterium glutamicum* constructed in Example 1.
    - (c) Search and identification of expressed protein effective in lysine production
    - [0475] It was found out that in Fig. 2A (ATCC 13032: wild type strain), Fig. 2B (FERM BP-7134: lysine-producing strain) and Fig. 2C (FERM BP-158: lysine-highly producing strain), the catalase corresponding to Spot-8 and the elongation factor Tu corresponding to Spot-9 as identified above showed the higher expression level with an increase in the lysine productivity.
    - [0476] Based on these results, it was found that hopeful mutated proteins can be efficiently searched and identified in breeding aiming at strengthening the productivity of a target product by the proteome analysis using the genome sequence database of *Corynebacterium glutamicum* constructed in Example 1.
- [0477] Moreover, useful mutation points of useful mutants can be easily specified by searching the nucleotide sequences (nucleotide sequences of promoter, ORF, or the like) relating to the identified proteins using the above database and using primers designed on the basis of the sequences. As a result of the fact that the mutation points are specified, industrially useful mutants which have the useful mutations or other useful mutations derived therefrom can be easily bred.
- <sup>45</sup> [0478] While the invention has been described in detail and with reference to specific embodiments thereof, it will be apparent to one of skill in the art that various changes and modifications can be made therein without departing from the spirit and scope thereof. All references cited herein are incorporated in their entirety.

#### Claims

15

20

25

30

35

40

50

- 1. A method for at least one of the following:
  - (A) identifying a mutation point of a gene derived from a mutant of a coryneform bacterium,
  - (B) measuring an expression amount of a gene derived from a coryneform bacterium,
  - (C) analyzing an expression profile of a gene derived from a coryneform bacterium,
  - (D) analyzing expression patterns of genes derived from a coryneform bacterium, or
  - (E) identifying a gene homologous to a gene derived from a coryneform bacterium,

said method comprising:

5

10

15

20

25

30

35

45

55

- (a) producing a polynucleotide array by adhering to a solid support at least two polynucleotides selected from the group consisting of first polynucleotides comprising the nucleotide sequence represented by any one of SEQ ID NOS:1 to 3501, second polynucleotides which hybridize with the first polynucleotides under stringent conditions, and third polynucleotides comprising a sequence of 10 to 200 continuous bases of the first or second polynucleotides.
- (b) incubating the polynucleotide array with at least one of a labeled polynucleotide derived from a coryneform bacterium, a labeled polynucleotide derived from a mutant of the coryneform bacterium or a labeled polynucleotide to be examined, under hybridization conditions,
- (c) detecting any hybridization, and
- (d) analyzing the result of the hybridization.
- 2. The method according to claim 1, wherein the coryneform bacterium is a microorganism belonging to the genus Corynebacterium, the genus Brevibacterium, or the genus Microbacterium.
- 3. The method according to claim 2, wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium ammoniagenes.
- 4. The method according to claim 1, wherein the polynucleotide derived from a coryneform bacterium, the polynucleotide derived from a mutant of the coryneform bacterium or the polynucleotide to be examined is a gene relating to the biosynthesis of at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof.
- 5. The method according to claim 1, wherein the polynucleotide to be examined is derived from Escherichia coli.
- 6. A polynucleotide array, comprising:

at least two polynucleotides selected from the group consisting of first polynucleotides comprising the nucleotide sequence represented by any one of SEQ ID NOS:1 to 3501, second polynucleotides which hybridize with the first polynucleotides under stringent conditions, and third polynucleotides comprising 10 to 200 continuous bases of the first or second polynucleotides, and a solid support adhered thereto.

- 7. A polynucleotide comprising the nucleotide sequence represented by SEQ ID NO:1 or a polynucleotide having a homology of at least 80% with the polynucleotide.
- 40 8. A polynucleotide comprising any one of the nucleotide sequences represented by SEQ ID NOS:2 to 3431, or a polynucleotide which hybridizes with the polynucleotide under stringent conditions.
  - 9. A polynucleotide encoding a polypeptide having any one of the amino acid sequences represented by SEQ ID NOS:3502 to 6931, or a polynucleotide which hybridizes therewith under stringent conditions.
  - 10. A polynucleotide which is present in the 5' upstream or 3' downstream of a polynucleotide comprising the nucleotide sequence of any one of SEQ ID NOS:2 to 3431 in a whole polynucleotide comprising the nucleotide sequence represented by SEQ ID NO:1, and has an activity of regulating an expression of the polynucleotide.
- 50 11. A polynucleotide comprising 10 to 200 continuous bases in the nucleotide sequence of the polynucleotide of any one of claims 7 to 10, or a polynucleotide comprising a nucleotide sequence complementary to the polynucleotide comprising 10 to 200 continuous based.
  - 12. A recombinant DNA comprising the polynucleotide of any one of claims 8 to 11.
  - 13. A transformant comprising the polynucleotide of any one of claims 8 to 11 or the recombinant DNA of claim 12.
  - 14. A method for producing a polypeptide, comprising:

#### EP 1 108 790 A2

culturing the transformant of claim 13 in a mildium to produce and accumulate a polypeptide encoded by the polynucleotide of claim 8 or 9 in the medium, and recovering this polypeptide from the medium.

5 15. A method for producing at least one of an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof, comprising:

culturing the transformant of claim 13 in a medium to produce and accumulate at least one of an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof in the medium, and recovering the at least one of the amino acid, the nucleic acid, the vitamin, the saccharide, the organic acid, and analogues thereof from the medium.

- **16.** A polypeptide encoded by a polynucleotide comprising the nucleotide sequence selected from SEQ ID NOS:2 to 3431.
- 17. A polypeptide comprising the amino acid sequence selected from SEQ ID NOS:3502 to 6931.
- 18. The polypeptide according to claim 16 or 17, wherein at least one amino acid is deleted, replaced, inserted or added, said polypeptides having an activity which is substantially the same as that of the polypeptide without said at least one amino acid deletion, replacement, insertion or addition.
- 19. A polypeptide comprising an amino acid sequence having a homology of at least 60% with the amino acid sequence of the polypeptide of claim 16 or 17, and having an activity which is substantially the same as that of the polypeptide.
- 25 20. An antibody which recognizes the polypeptide of any one of claims 16 to 19.
  - 21. A polypeptide array, comprising:

10

15

20

30

35

40

45

50

55

at least one polypeptide or partial fragment polypeptide selected from the polypeptides of claims 16 to 19 and partial fragment polypeptides of the polypeptides, and a solid support adhered thereto.

22. A polypeptide array, comprising:

at least one antibody which recognizes a polypeptide or partial fragment polypeptide selected from the polypeptides of claims 16 to 19 and partial fragment polypeptides of the polypeptides, and a solid support adhered thereto.

- 23. A system based on a computer for identifying a target sequence or a target structure motif derived from a coryneform bacterium, comprising the following:
  - (i) a user input device that inputs at least one nucleotide sequence information selected from SEQ ID NOS:1 to 3501, and target sequence or target structure motif information;
  - (ii) a data storage device for at least temporarily storing the input information;
  - (iii) a comparator that compares the at least one nucleotide sequence information selected from SEQ ID NOS: 1 to 3501 with the target sequence or target structure motif information, recorded by the data storage device for screening and analyzing nucleotide sequence information which is coincident with or analogous to the target sequence or target structure motif information; and
  - (iv) an output device that shows a screening or analyzing result obtained by the comparator.

24. A method based on a computer for identifying a target sequence or a target structure motif derived from a coryneform bacterium, comprising the following:

- (i) inputting at least one nucleotide sequence information selected from SEQ ID NOS:1 to 3501, target sequence information or target structure motif information into a user input device;
- (ii) at least temporarily storing said information;
- (iii) comparing the at least one nucleotide sequence information selected from SEQ ID NOS:1 to 3501 with the target sequence or target structure motif information; and

#### EP 1 108 790 A2

- (iv) screening and analyzing nucleotide sequence information which is coincident with or analogous to the target sequence or target structure motif information.
- 25. A system based on a computer for identifying a target sequence or a target structure motif derived from a coryneform bacterium, comprising the following:
  - (i) a user input device that inputs at least one amino acid sequence information selected from SEQ ID NOS: 3502 to 7001, and target sequence or target structure motif information;
  - (ii) a data storage device for at least temporarily storing the input information;
  - (iii) a comparator that compares the at least one amino acid sequence information selected from SEQ ID NOS: 3502 to 7001 with the target sequence or target structure motif information, recorded by the data storage device for screening and analyzing amino acid sequence information which is coincident with or analogous to the target sequence or target structure motif information; and
  - (iv) an output device that shows a screening or analyzing result obtained by the comparator.
- 26. A method based on a computer for identifying a target sequence or a target structure motif derived from a coryneform bacterium, comprising the following:
  - (i) inputting at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001, and target sequence information or target structure motif information into a user input device;
  - (ii) at least temporarily storing said information;

5

10

15

20

25

30

35

45

50

- (iii) comparing the at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001 with the target sequence or target structure motif information; and
- (iv) screening and analyzing amino acid sequence information which is coincident with or analogous to the target sequence or target structure motif information.
- 27. A system based on a computer for determining a function of a polypeptide encoded by a polynucleotide having a target nucleotide sequence derived from a coryneform bacterium, comprising the following:
  - (i) a user input device that inputs at least one nucleotide sequence information selected from SEQ ID NOS:2 to 3501, function information of a polypeptide encoded by the nucleotide sequence, and target nucleotide sequence information;
  - (ii) a data storage device for at least temporarily storing the input information;
  - (iii) a comparator that compares the at least one nucleotide sequence information selected from SEQ ID NOS: 2 to 3501 with the target nucleotide sequence information for determining a function of a polypeptide encoded by a polynucleotide having the target nucleotide sequence which is coincident with or analogous to the polynucleotide having at least one nucleotide sequence selected from SEQ ID NOS:2 to 3501; and
  - (iv) an output devices that shows a function obtained by the comparator.
- 28. A method based on a computer for determining a function of a polypeptide encoded by a polypeptide encoded by a polypucleotide having a target nucleotide sequence derived from a coryneform bacterium, comprising the following:
  - (i) inputting at least one nucleotide sequence information selected from SEQ ID NOS:2 to 3501, function information of a polypeptide encoded by the nucleotide sequence, and target nucleotide sequence information;
  - (ii) at least temporarily storing said information;
  - (iii) comparing the at least one nucleotide sequence information selected from SEQ ID NOS:2 to 3501 with the target nucleotide sequence information; and
  - (iv) determining a function of a polypeptide encoded by a polynucleotide having the target nucleotide sequence which is coincident with or analogous to the polynucleotide having at least one nucleotide sequence selected from SEQ ID NOS:2 to 3501.
  - 29. A system based on a computer for determining a function of a polypeptide having a target amino acid sequence derived from a coryneform bacterium, comprising the following:
    - (i) a user input device that inputs at least one amino acid sequence information selected from SEQ ID NOS: 3502 to 7001, function information based on the amino acid sequence, and target amino acid sequence information;

- (ii) a data storing device for at least temporarily storing the input information;
- (iii) a comparator that compares the at least one amino acid sequence information selected from SEQ ID NOS: 3502 to 7001 with the target amino acid sequence information for determining a function of a polypeptide having the target amino acid sequence which is coincident with or analogous to the polypeptide having at least one amino acid sequence selected from SEQ ID NOS:3502 to 7001; and
- (iv) an output device that shows a function obtained by the comparator.
- **30.** A method based on a computer for determining a function of a polypeptide having a target amino acid sequence derived from a coryneform bacterium, comprising the following:
  - (i) inputting at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001, function information based on the amino acid sequence, and target amino acid sequence information;
  - (ii) at least temporarily storing said information;

10

15

25

30

35

50

- (iii) comparing the at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001 with the target amino acid sequence information; and
- (iv) determining a function of a polypeptide having the target amino acid sequence which is coincident with or analogous to the polypeptide having at least one amino acid sequence selected from SEQ ID NOS:3502 to 7001.
- 31. The system according to any one of claims 23, 25, 27 and 29, wherein a coryneform bacterium is a microorganism of the genus Corynebacterium, the genus Brevibacterium, or the genus Microbacterium.
  - **32.** The method according to any one of claims 24, 26, 28 and 30, wherein a coryneform bacterium is a microorganism of the genus *Corynebacterium*, the genus *Brevibacterium*, or the genus *Microbacterium*.
  - 33. The system according to claim 31, wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium ammoniagenes.
  - 34. The method according to claim 32, wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium ammoniagenes.
  - 35. A recording medium or storage device which is readable by a computer in which at least one nucleotide sequence information selected from SEQ ID NOS:1 to 3501 or function information based on the nucleotide sequence is recorded, and is usable in the system of claim 23 or 27 or the method of claim 24 or 28.
- 36. A recording medium or storage device which is readable by a computer in which at least one amino acid sequence information selected from SEQ ID NOS:3502 to 7001 or function information based on the amino acid sequence is recorded, and is usable in the system of claim 25 or 29 or the method of claim 26 or 30.
- 37. The recording medium or storage device according to claim 35 or 36, which is a computer readable recording medium selected from the group consisting of a floppy disc, a hard disc, a magnetic tape, a random access memory (RAM), a read only memory (ROM), a magneto-optic disc (MO), CD-ROM, CD-R, CD-RW, DVD-ROM, DVD-RAM and DVD-RW.
  - **38.** A polypeptide having a homoserine dehydrogenase activity, comprising an amino acid sequence in which the Val residue at the 59th in the amino acid sequence of homoserine dehydrogenase derived from a coryneform bacterium is replaced with an amino acid residue other than a Val residue.
  - 39. A polypeptide comprising an amino acid sequence in which the Val residue at the 59th position in the amino acid sequence as represented by SEQ ID NO:6952 is replaced with an amino acid residue other than a Val residue.
  - 40. The polypeptide according to claim 38 or 39, wherein the Val residue at the 59th position is replaced with an Ala residue.

- 41. A polypeptide having pyruvate carboxylase activity, comprising an amino acid sequence in which the Pro residue at the 458th position in the amino acid sequence of pyruvate carboxylase derived from a coryneform bacterium is replaced with an amino acid residue other than a Pro residue.
- 42. A polypeptide comprising an amino acid sequence in which the Pro residue at the 458th position in the amino acid sequence represented by SEQ ID NO:4265 is replaced with an amino acid residue other than a Pro residue.
  - 43. The polypeptide according to claim 41 or 42, wherein the Pro residue at the 458th position is replaced with a Ser residue.
  - 44. The polypeptide according to any one of claims 38 to 43, which is derived from Corynebacterium glutamicum.
  - 45. A DNA encoding the polypeptide of any one of claims 38 to 44.
- 46. A recombinant DNA comprising the DNA of claim 45.
  - 47. A transformant comprising the recombinant DNA of claim 46.
  - 48. A transformant comprising in its chromosome the DNA of claim 45.
  - 49. The transformant according to claim 47 or 48, which is derived from a coryneform bacterium.
  - 50. The transformant according to claim 49, which is derived from Corynebacterium glutamicum.
- 25. 51. A method for producing L-lysine, comprising:

10

15

20

30

35

40

45

55

culturing the transformant of any one of claims 47 to 50 in a medium to produce and accumulate L-lysine in the medium, and recovering the L-lysine from the culture.

- **52.** A method for breeding a coryneform bacterium using the nucleotide sequence information represented by SEQ ID NOS:1 to 3431, comprising the following:
  - (i) comparing a nucleotide sequence of a genome or gene of a production strain derived a coryneform bacterium which has been subjected to mutation breeding so as to produce at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogous thereof by a fermentation method, with a corresponding nucleotide sequence in SEQ ID NOS:1 to 3431;
  - (ii) identifying a mutation point present in the production strain based on a result obtained by (i);
  - (iii) introducing the mutation point into a coryneform bacterium which is free of the mutation point, or deleting the mutation point from a coryneform bacterium having the mutation point; and
  - (iv) examining productivity by the fermentation method of the compound selected in (i) of the coryneform bacterium obtained in (iii).
- 53. The method according to claim 52, wherein the gene is a gene encoding an enzyme in a biosynthetic pathway or a signal transmission pathway.
- 54. The method according to claim 52, wherein the mutation point is a mutation point relating to a useful mutation which improves or stabilizes the productivity.
- 50 55. A method for breading a coryneform bacterium using the nucleotide sequence information represented by SEQ ID NOS:1 to 3431, comprising:
  - (i) comparing a nucleotide sequence of a genome or gene of a production strain derived a coryneform bacterium which has been subjected to mutation breeding so as to produce at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogous thereof by a fermentation method, with a corresponding nucleotide sequence in SEQ ID NOS:1 to 3431;
  - (ii) identifying a mutation point present in the production strain based on a result obtain by (i);
  - (iii) deleting a mutation point from a coryneform bacterium having the mutation point; and

#### EP 1 108 790 A2

- (iv) examining productivity by the fermentation method of the compound selected in (i) of the coryneform bacterium obtained in (iii).
- 56. The method according to claim 55, wherein the gene is a gene encoding an enzyme in a biosynthetic pathway or a signal transmission pathway.
- 57. The method according to claim 55, wherein the mutation point is a mutation point which decreases or destabilizes the productivity.
- 58. A method for breeding a coryneform bacterium using the nucleotide sequence information represented by SEQ ID NOS:2 to 3431, comprising the following:
  - (i) identifying an isozyme relating to biosynthesis of at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogous thereof, based on the nucleotide sequence information represented by SEQ ID NOS:2 to 3431;
  - (ii) classifying the isozyme identified in (i) into an isozyme having the same activity;
  - (iii) mutating all genes encoding the isozyme having the same activity simultaneously; and
  - (iv) examining productivity by a fermentation method of the compound selected in (i) of the coryneform bacterium which have been transformed with the gene obtained in (iii).
  - 59. A method for breeding a coryneform bacterium using the nucleotide sequence information represented by SEQ ID NOS:2 to 3431, comprising the following:
    - (i) arranging a function information of an open reading frame (ORF) represented by SEQ ID NOS:2 to 3431;
    - (ii) allowing the arranged ORF to correspond to an enzyme on a known biosynthesis or signal transmission pathway;
    - (iii) explicating an unknown biosynthesis pathway or signal transmission pathway of a coryneform bacterium in combination with information relating known biosynthesis pathway or signal transmission pathway of a coryneform bacterium;
    - (iv) comparing the pathway explicated in (iii) with a biosynthesis pathway of a target useful product; and
    - (v) transgenetically varying a coryneform bacterium based on the nucleotide sequence information to either strengthen a pathway which is judged to be important in the biosynthesis of the target useful product in (iv) or weaken a pathway which is judged not to be important in the biosynthesis of the target useful product in (iv).
- 35 **60.** A coryneform bacterium, bred by the method of any one of claims 52 to 59.
  - 61. The coryneform bacterium according to claim 60, which is a microorganism belonging to the genus *Corynebacterium*, the genus *Brevibacterium*, or the genus *Microbacterium*.
- 62. The coryneform bacterium according to claim 61, wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium herculis, corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoamino genes, and Corynebacterium ammonia genes.
  - **63.** A method for producing at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid and an analogue thereof, comprising:
    - culturing a coryneform bacterium of any one of claims 60 to 62 in a medium to produce and accumulate at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof;
    - recovering the compound from the culture.
  - 64. The method according to claim 63, wherein the compound is L-lysine.
  - 65. A method for identifying a protein relating to useful mutation based on proteome analysis, comprising the following:
    - (i) preparing

5

15

20

25

30

50

# EP 1 108 790 A2

a protein derived from a bacterium of a production strain of a coryneform bacterium which has been subjected to mutation breeding by a fermentation process so as to produce at least one compound selected from an amino acid, a nucleic acid, a vitamin, a saccharide, an organic acid, and analogues thereof, and a protein derived from a bacterium of a parent strain of the production strain;

5

10

- (ii) separating the proteins prepared in (i) by two dimensional electrophoresis;
- (iii) detecting the separated proteins, and comparing an expression amount of the protein derived from the production strain with that derived from the parent strain;
- (iv) treating the protein showing different expression amounts as a result of the comparison with a peptidase to extract peptide fragments;
- (v) analyzing amino acid sequences of the peptide fragments obtained in (iv); and
- (vi) comparing the amino acid sequences obtained in (v) with the amino acid sequence represented by SEQ
- ID NOS:3502 to 7001 to identifying the protein having the amino acid sequences.
- 66. The method according to claim 65, wherein the coryneform bacterium is a microorganism belonging to the genus corynebacterium, the genus Brevibacterium, or the genus Microbacterium.
  - 67. The method according to claim 66, wherein the microorganism belonging to the genus Corynebacterium is selected from the group consisting of Corynebacterium glutamicum, Corynebacterium acetoglutamicum, Corynebacterium callunae, Corynebacterium herculis, Corynebacterium lilium, Corynebacterium melassecola, Corynebacterium thermoaminogenes, and Corynebacterium ammoniagenes.
  - 68. A biologically pure culture of Corynebacterium glutamicum AHP-3 (FERM BP-7382) .

25

20

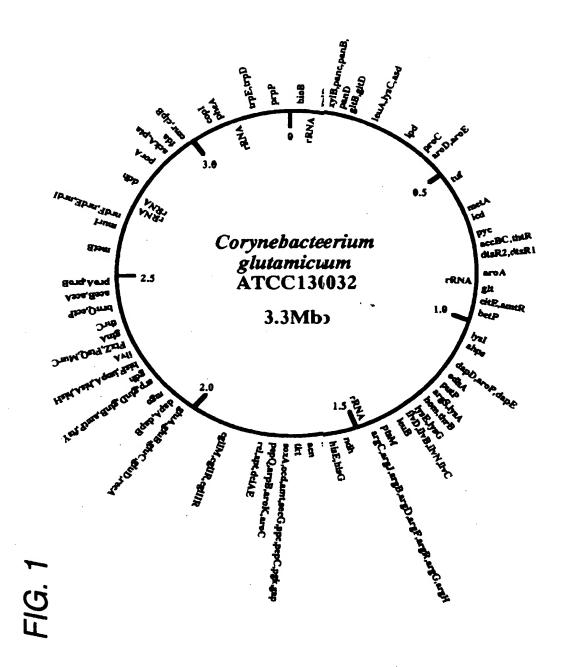
30

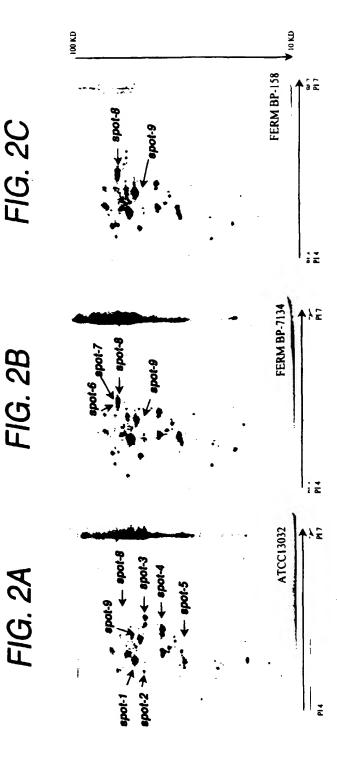
35

40

45

50





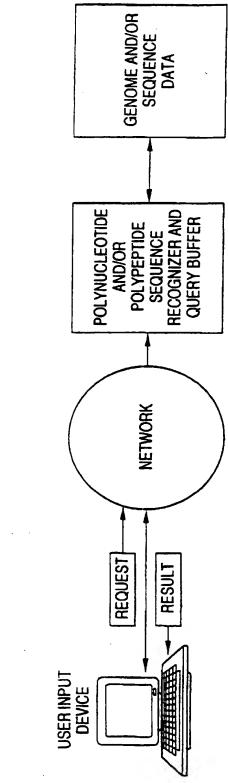


FIG. 3

FIG. 4

